Ag(I)-Catalyzed Asymmetric (2 + 4) Annulation Reaction of 5-Alkenyl Thiazolones: Synthesis of Enantioenriched Spiro[cyclohexenamines-thiazolone]

Kavita Choudhary, Akanksha Santosh Deshpande, and Vinod K. Singh*

[a]Department of Chemistry, Indian Institute of Technology Kanpur, Kanpur-208016, Uttar Pradesh (India)

*E-mail: vinodks@iitk.ac.in

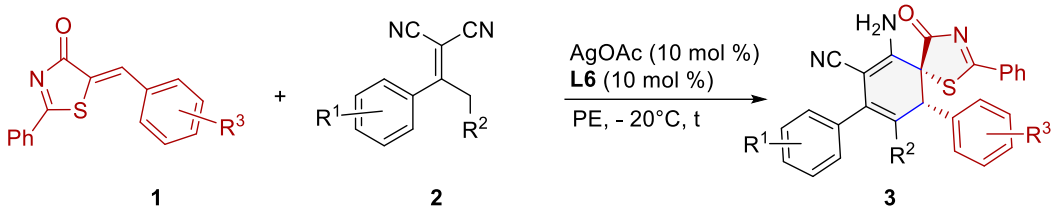
Contents:

General information

All reactions were carried out in oven-dried glassware with magnetic stirring. ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were recorded on Joel (500 MHz and 400 MHz) spectrometers in $CDCl_3$. Chemical shifts are reported in delta (δ) units, in parts per million (ppm). Tetramethylsilane or residual solvent peak was used as an internal standard for ^{1}H and $^{13}C\{^{1}H\}$ NMR, respectively. Coupling constants were reported in Hz. Splitting patterns are designated as s for singlet, d for doublet, t for triplet, q for a quartet, dd for doublet of doublet, and m for multiplet. Mass spectrometric analysis was done using the ESI-TOF method. Routine monitoring of reactions was performed using precoated silica gel TLC plates from E-Merck. All the chromatographic separations were carried out using silica gel (Merck's, 100–200 mesh). Enantiomeric excess was determined by HPLC analysis using Daicel chiral columns at 25 ºC. Optical rotations were measured on a commercially available automatic polarimeter. Melting points were recorded on a digital melting point apparatus. α,α-Dicyanoalkenes **(1)**[1,] and 5-alkenyl thiazolones **(2)**[2] were prepared by the previously reported methods.

Compound **3aa** was crystallized by slow evaporation of DCM/Hexane (1:1). The X-ray crystallography data of **3aa** was collected on a Bruker SMART APEX CCD diffractometer equipped with CRYO Industries low-temperature apparatus, and intensity data were collected using graphite-monochromated Mo Kα radiation (λ= 0.71073 Å) at 100 K. The CCDC number of compounds **3aa:** 2359432 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK; fax: (+44)1223- 336-033; or (deposit@ccdc.cam.ac.uk).

Synthetic procedure (A) for asymmetric annulation reactions:

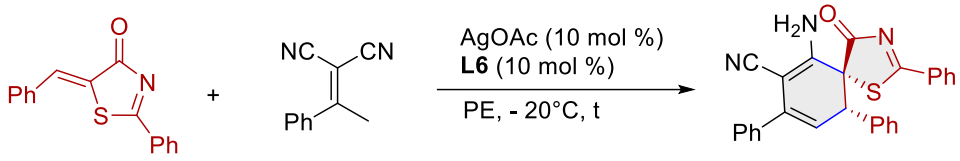


1 **2** **3**

In an oven-dried round bottom flask equipped with a magnetic stir bar, Ag(OAc) (10 mol %, 1.6 mg, 0.01 mmol), ligand **L6** (10 mol %, 11.7 mg, 0.01 mmol) were taken, and 2 mL petroleum ether (PE) was added to it. The reaction mixture was stirred for 1 hour at room temperature. The round bottom flask containing the catalyst mixture was then cooled down to -20 °C. 5-alkenyl thiazolones, **1** (0.1 mmol, 1.0 equiv) and α,α-Dicyanoalkenes, **2** (0.15 mmol, 1.5 equiv) were added sequentially into the reaction mixture and continued stirring at the same temperature (-20 °C). After the complete consumption of the starting material (monitored by TLC), the reaction mixture was passed through a small silica pad to remove the catalyst. The resulting mixture was purified by flash column chromatography to get pure product **3**.

Notes: The diastereomeric ratio was determined by ^{1}H NMR of the crude reaction mixture. Racemic samples were prepared using the same procedure using AgOAc (10 mol %) with racemic BINAP (10 mol %).

Procedure for 2 mmol scale-up reaction:

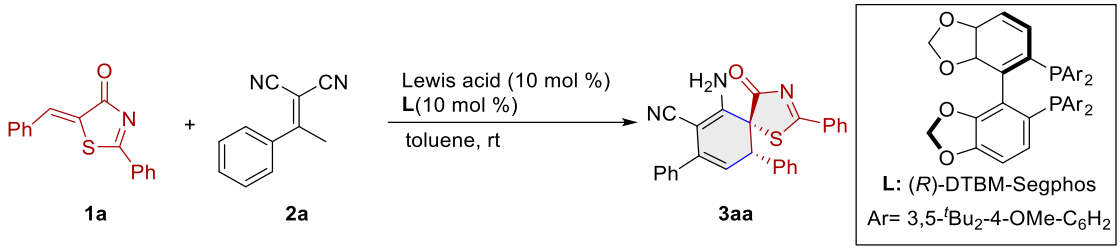


1a **2a** **3aa**

In an oven-dried round bottom flask equipped with a magnetic stir bar, Ag(OAc) (10 mol %, 33.3 mg, 0.2 mmol), ligand **L6** (10 mol %, 235.9 mg, 0.2 mmol) were taken, and 5 mL petroleum ether was added to it. The reaction mixture was stirred for 1 hour at room temperature. The round bottom flask containing the catalyst mixture was then cooled down to -20 °C. **1a** (530.6 mg, 2.0 mmol, 1.0 equiv) and **2a** (504.57 mg, 3.0 mmol, 1.5 equiv) were added sequentially into the reaction mixture and continued stirring at the same temperature (-20 °C). After the complete consumption of the starting material (monitored by TLC), the reaction mixture was passed through a small silica pad to remove the catalyst. The resulting mixture was purified by flash column chromatography to get pure product **3aa** in 78% yield (676 mg). **HPLC: 97% ee,** (IC, IPA/n-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 25.04 min (major), 32.69 min (minor).

Detailed optimization studies:

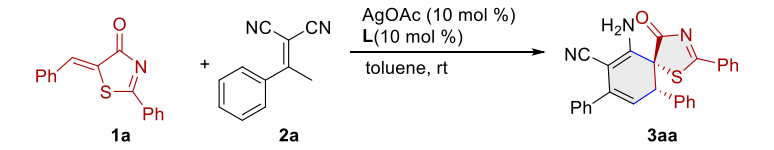
Table S1. Evaluation of Lewis acids

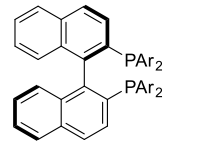


Entry	Lewis acid	Time (h)	Yield[b] (%)	ee[c] (%)	dr[d]
1	$Ag(OCOCF_3)$	7	85	79	>20:1
2	AgOAc	6	96	89	>20:1
3	$Ag(NO_3)$	8	75	35	>20:1
4	Ag(OTf)	12	79	75	>20:1
5	Ag_2CO_3	12	85	80	>20:1
6	Cu(OAc)	24	78	20	>20:1
7	$Cu(OTf)_2$	48	68	55	>20:1
8	AgF	72	56	54	>20:1
9	AgI	48	trace	-	-

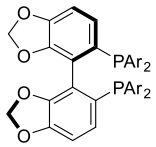
[a]Reaction conditions: **1a** (26.5 mg, 0.1 mmol, 1.0 equiv), **2a** (16.8 mg, 0.15 mmol, 1.5 equiv), **L** (10 mol %, 0.10 equiv) Lewis acid (10 mol %, 0.10 equiv), toluene (1.0 mL), rt. [b]Isolated yield. [c]Determined by chiral HPLC. [d]Diastereomeric ratio (dr) determined by ^{1}H NMR of crude reaction mixture.

Table S2. Evaluation of ligands

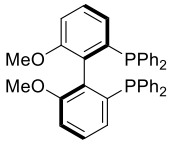




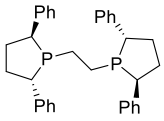
L1 : Ar= Ph
L2: Ar= 4-Me-C_6H_4
L3: Ar= 3,5-Me_2-C_6H_3



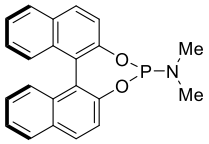
L4 : Ar= Ph
L5: Ar= 3,5-Me_2-C_6H_3
L6: Ar= 3,5-^{t}Bu$_2$-4-OMe-C_6H_2



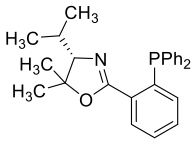
L7



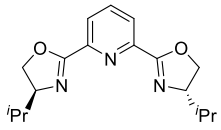
L8



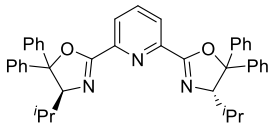
L9



L10



L11



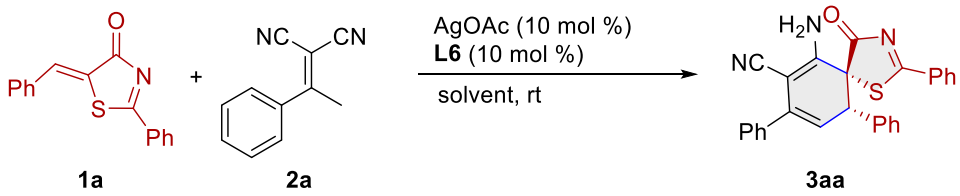
L12

Entry	Ligand	Time (h)	Yield[b] (%)	ee[c] (%)	dr[d]
1	**L1**	4	80	46	>20:1
2	**L2**	5	81	67	>20:1
3	**L3**	7	51	47	>20:1
4	**L4**	5	85	44	>20:1
5	**L5**	6	89	76	>20:1
6	**L6**	6	96	89	>20:1

7	**L7**	8	82	53	>20:1
8	**L8**	8	78	44	>20:1
9	**L9**	5	65	30	>20:1
10	**L10**	8	70	28	>20:1
11	**L11**	24	60	20	>20:1
12	**L12**	72	trace	-	-

[a]Reaction conditions: **1a** (26.5 mg, 0.1 mmol, 1.0 equiv), **2a** (16.8 mg, 0.15 mmol, 1.5 equiv), **L** (10 mol %, 0.10 equiv), AgOAc (1.6 mg, 10 mol %, 0.10 equiv), toluene (1.0 mL), rt. [b]Isolated yield. [c]Determined by chiral HPLC. [d]Diastereomeric ratio (dr) determined by ^{1}H NMR of crude reaction mixture.

Table S3. Solvent screening

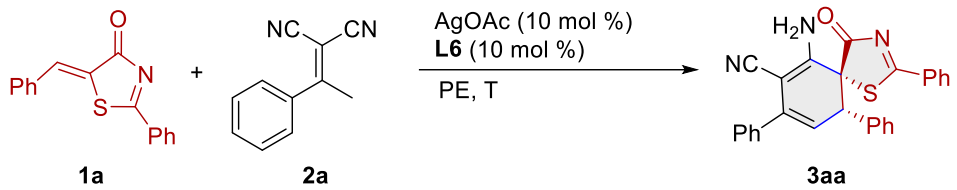


1a **2a** **3aa**

Entry	Solvent	Time(h)	Yield[b] (%)	ee[c] (%)	dr[d]
1	toluene	6	96	89	>20:1
2	$PhCF_3$	12	80	83	>20:1
3	PhCl	18	95	88	>20:1
4	PhF	22	79	63	>20:1
5	1,4-dioxane	22	70	38	>20:1
6	*p*-xylene	24	60	10	>20:1
7	Et_2O	18	85	82	>20:1
8	tert butyl methyl ether	24	65	56	>20:1
9	THF	18	70	60	>20:1
10	CH_3CN	24	78	38	>20:1
11	EtOAc	20	80	79	>20:1
12	DCM	72	trace	-	>20:1
13	CCl_4	20	88	80	>20:1
14	DCE	18	78	62	>20:1
15	hexane	20	95	88	>20:1
16	cyclohexane	22	78	79	>20:1
17	heptane	20	80	86	>20:1
18	pentane	20	82	83	>20:1
19	petroleum ether	22	96	91	>20:1

[a]Reaction conditions: **1a** (26.5 mg, 0.1 mmol, 1.0 equiv), **2a** (16.8 mg, 0.15 mmol, 1.5 equiv), **L6** (11.7 mg, 10 mol %, 0.10 equiv), AgOAc (1.6 mg, 10 mol %, 0.10 equiv), solvent (1.0 mL), rt. [b]Isolated yield. [c]Determined by chiral HPLC. [d]Diastereomeric ratio (dr) determined by ^{1}H NMR of crude reaction mixture.

Table S4. Effect of temperature

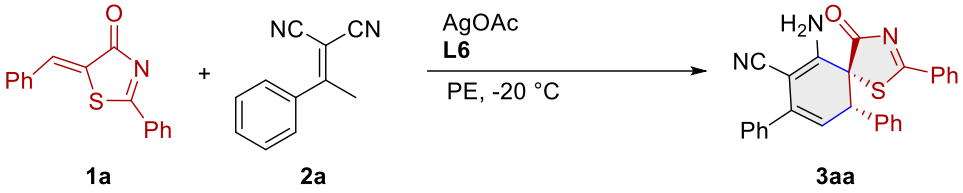


1a 2a 3aa

Entry	T (°C)	Time (h)	Yield[b] (%)	ee[c] (%)	dr[d]
1	rt	22	96	91	>20:1
2	0	30	90	90	>20:1
3	-10	35	88	92	>20:1
4	-20	45	80	96	>20:1

[a]Reaction conditions: **1a** (26.5 mg, 0.1 mmol, 1.0 equiv), **2a** (16.8 mg, 0.15 mmol, 1.5 equiv), **L6** (11.7 mg, 10 mol %, 0.10 equiv), AgOAc (1.6 mg, 10 mol %, 0.10 equiv), Petroleum ether (PE) (1.0 mL). [b]Isolated yield. [c]Determined by chiral HPLC. [d]Diastereomeric ratio (dr) determined by ^{1}H NMR of the crude reaction mixture. PE: Petroleum ether

Table S5. Effect of catalyst loading



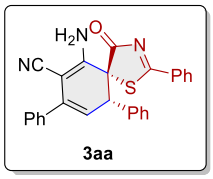
1a 2a 3aa

Entry	Ag(OCOCF$_3$) (mol %)	L6 (mol %)	Time(h)	Yield[b] (%)	ee[c] (%)	dr[d]
1	10	10	45	80	96	>20:1
2	5	5	72	90	90	>20:1
3	2	2	80	88	92	>20:1

[a]Reaction conditions: **1a** (26.5 mg, 0.1 mmol, 1.0 equiv), **2a** (16.8 mg, 0.15 mmol, 1.5 equiv), **L6**, AgOAc, Petroleum ether (PE) (1.0 mL). [b]Isolated yield. [c]Determined by chiral HPLC. [d]Diastereomeric ratio (dr) determined by ^{1}H NMR of the crude reaction mixture. PE: Petroleum ether

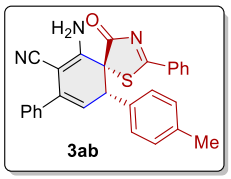
Characterization of annulated products 3:

(5*R*,10*S*)-6-amino-4-oxo-2,8,10-triphenyl-1-thia-3-azaspiro[4.5]deca-2,6,8-triene-7-carbonitrile (3aa):



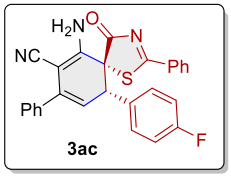
The compound was prepared following the synthetic procedure A. The desired product was isolated by flash column chromatography (15:85 = EtOAc/Hexanes, v/v) to afford a yellow solid (34.6 mg, 80% yield). $[\alpha]_D^{20}$ = + 62.8 (c = 0.5, $CHCl_3$). **HPLC**: **96% ee**, (IC, IPA/n-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 24.95 min (major), 32.44 min (minor). **mp**: 188-190 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.80 (d, *J* = 7.8 Hz, 2H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.48 – 7.44 (m, 2H), 7.40 (dd, *J* = 7.6, 5.4 Hz, 4H), 7.37 – 7.33 (m, 3H), 7.18 (dd, *J* = 5.0, 2.2 Hz, 3H), 5.88 (d, *J* = 2.7 Hz, 1H), 5.32 (s, 2H), 4.61 (d, *J* = 2.9 Hz, 1H). **^{13}C{^{1}H } NMR (100 MHz, $CDCl_3$)** δ 197.2, 191.5, 155.0, 137.6, 137.3, 135.9, 135.5, 131.4, 130.3, 129.2, 128.9, 128.74, 128.68, 128.5, 128.3, 127.7, 120.9, 117.2, 83.5, 74.2, 50.4. **HRMS (ESI, m/z):** $[M + Na]^+$ calculated for $C_{27}H_{19}N_3NaOS^+$: 456.1142; found: 434.1144.

(5*R*,10*S*)-6-amino-4-oxo-2,8-diphenyl-10-(p-tolyl)-1-thia-3-azaspiro[4.5]deca-2,6,8-triene-7 carbonitrile (3ab):



The compound was prepared following the synthetic procedure A. The desired product was isolated by flash column chromatography (15:85 = EtOAc/Hexanes, v/v) to afford a yellow semi-solid (31.3 mg, 70% yield). $[\alpha]_D^{20}$ = + 66.8 (c = 0.5, $CHCl_3$). **mp**: 188-190 °C. **HPLC**: **92% ee**, (IC, IPA/n-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 28.82 min (major), 37.62 min (minor). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.99 (d, *J* = 7.6 Hz, 2H), 7.76 (t, *J* = 7.5 Hz, 1H), 7.62 – 7.50 (m, 7H), 7.41 – 7.34 (m, 2H), 7.14 (d, *J* = 7.8 Hz, 2H), 6.01 (d, *J* = 2.8 Hz, 1H), 5.41 (s, 2H), 4.71 (d, *J* = 2.9 Hz, 1H), 2.34 (s, 3H). **^{13}C{^{1}H } NMR (100 MHz, $CDCl_3$)** δ 197.2, 191.5, 155.2, 138.2, 137.7, 137.2, 135.8, 132.4, 131.5, 130.1, 129.2, 129.0, 128.9, 128.6, 127.6, 121.2, 117.2, 83.3, 74.4, 49.9, 21.2. **HRMS (ESI, m/z):** $[M + H]^+$ calculated for $C_{28}H_{22}N_3OS^+$: 448.1479; found: 448.1465

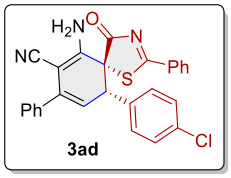
(5*R*,10*S*)-6-amino-10-(4-fluorophenyl)-4-oxo-2,8-diphenyl-1-thia-3-azaspiro[4.5]deca-2,6,8-triene-7-carbonitrile (3ac):



The compound was prepared following the synthetic procedure A. The desired product was isolated by flash column chromatography (15:85 = EtOAc/Hexanes, v/v) to afford a yellow solid (30.7 mg, 68% yield).

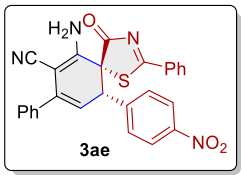
[α]$_D^{20}$ = + 49.3 (c = 0.45, $CHCl_3$). **HPLC**: **97% ee**, (IC, IPA/n-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 19.05 min (major), 31.51 min (minor). **mp**: 187-189 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.86 (d, *J* = 7.7 Hz, 2H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.47 – 7.38 (m, 7H), 7.34 (dd, *J* = 8.7, 5.3 Hz, 2H), 6.89 (t, *J* = 8.7 Hz, 2H), 5.83 (d, *J* = 2.9 Hz, 1H), 5.15 (s, 2H), 4.59 (d, *J* = 2.8 Hz, 1H). **^{13}C {^{1}H } NMR (125 MHz, $CDCl_3$)** δ 197.3, 191.5, δ 162.70 (d, *J* = 247.8 Hz), 154.9, 137.6, 137.5, 136.1, 131.96 (d, *J* = 8.3 Hz), 129.3, 129.0, 128.7, 127.7, 120.6, 117.0, 115.34 (d, *J* = 21.1 Hz), 83.8, 74.3, 49.6. **^{19}F{^{1}H } NMR (471 MHz, $CDCl_3$)** δ -113.05 **HRMS (ESI, m/z):** $[M + H]^+$ calculated for $C_{27}H_{19}FN_3OS^+$: 452.1228; found: 452.1234.

(5*R*,10*S*)-6-amino-10-(4-chlorophenyl)-4-oxo-2,8-diphenyl-1-thia-3-azaspiro[4.5]deca-2,6,8-triene-7-carbonitrile (3ad):



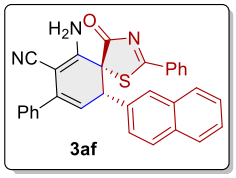
The compound was prepared following the synthetic procedure A. The desired product was isolated by flash column chromatography (15:85 = EtOAc/Hexanes, v/v) to afford a yellow solid (33.7 mg, 72% yield). **[α]**$_D^{20}$ = + 46.4 (c = 0.37, $CHCl_3$). **HPLC**: **90% ee**, (IC, IPA/n-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 18.11 min (major), 29.84 min (minor). **mp**: 199-201°C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.86 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.68 – 7.60 (m, 1H), 7.48 – 7.36 (m, 7H), 7.30 (d, *J* = 6.6 Hz, 2H), 7.17 (d, *J* = 8.5 Hz, 2H), 5.80 (d, *J* = 2.9 Hz, 1H), 5.26 (s, 2H), 4.58 (d, *J* = 2.8 Hz, 1H). **^{13}C {^{1}H } NMR (125 MHz, $CDCl_3$)** δ 197.3, 191.3, 155.0, 137.8, 137.5, 136.2, 134.5, 134.1, 131.6, 131.3, 129.3, 129.0, 128.8, 128.7, 128.6, 127.6, 120.1, 117.0, 83.4, 74.0, 49.6. **HRMS (ESI, m/z):** $[M + H]^+$ calculated for $C_{27}H_{19}ClN_3OS^+$: 468.0932; found: 468.0924.

(5*R*,10*S*)-6-amino-10-(4-nitrophenyl)-4-oxo-2,8-diphenyl-1-thia-3-azaspiro[4.5]deca-2,6,8-triene-7-carbonitrile (3ae):



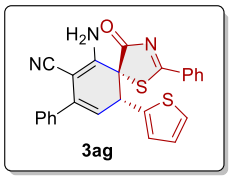
The compound was prepared following the synthetic procedure A. The desired product was isolated by flash column chromatography (20:80 = EtOAc/Hexanes, v/v) to afford a yellow solid (31.1mg, 65% yield). **[α]**$_D^{20}$ = + 45.2 (c = 0.42, $CHCl_3$). **HPLC**: **85% ee**, (IC, IPA/n-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 36.81 min (major), 65.58 min (minor). **mp**: 202-204 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.07 (d, *J* = 8.5 Hz, 2H), 7.86 (d, *J* = 7.9 Hz, 2H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.56 (d, *J* = 8.6 Hz, 2H), 7.47 – 7.43 (m, 5H), 7.43 (s, 2H), 5.81 (d, *J* = 2.7 Hz, 1H), 5.18 (s, 2H), 4.73 (d, *J* = 2.8 Hz, 1H). **^{13}C{^{1}H } NMR (100 MHz, $CDCl_3$)** δ 197.3, 190.9, 154.7, 147.9, 143.1, 138.4, 137.2, 136.6, 131.4, 131.0, 129.6, 129.5, 129.3, 129.1, 128.9, 128.8, 127.7, 123.5, 118.6, 116.7, 83.8, 73.7, 49.8. **HRMS (ESI, m/z):** $[M + H]^+$ calculated for $C_{27}H_{19}N_4O_3S^+$: 479.1173; found: 479.1171.

(5*R*,10*S*)-6-amino-10-(naphthalen-2-yl)-4-oxo-2,8-diphenyl-1-thia-3-azaspiro[4.5]deca-2,6,8-triene-7-carbonitrile (3af):



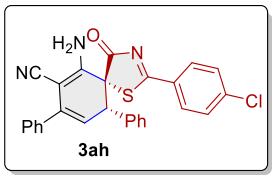
The compound was prepared following the synthetic procedure A. The desired product was isolated by flash column chromatography (15:85 = EtOAc/Hexanes, v/v) to afford a yellow solid (33.8 mg, 70% yield). $[\alpha]_D^{20}$ = + 66.9 (c = 0.62, $CHCl_3$). **HPLC**: **82% ee**, (IC, IPA/n-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 31.41 min (major), 39.46 min (minor). **mp**: 199-201 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.86 – 7.77 (m, 3H), 7.76 – 7.67 (m, 3H), 7.55 (d, *J* = 7.4 Hz, 1H), 7.53 – 7.46 (m, 3H), 7.46 – 7.38 (m, 5H), 7.35 (t, *J* = 7.8 Hz, 2H), 6.00 (d, *J* = 2.9 Hz, 1H), 5.17 (s, 2H), 4.79 (d, *J* = 2.9 Hz, 1H). **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)** δ 197.2, 191.4, 155.1, 137.6, 137.4, 135.9, 133.2, 133.1, 133.0, 131.4, 129.9, 129.1, 128.9, 128.8, 128.7, 128.2, 128.0, 127.8, 127.7, 127.6, 126.4, 126.3, 121.1, 117.1, 83.8, 74.4, 50.2. **HRMS (ESI, m/z):** $[M + H]^+$ calculated for $C_{31}H_{22}N_3OS^+$: 484.1479; found: 484.1478

(5*R*,10*S*)-6-amino-4-oxo-2,8-diphenyl-10-(thiophen-2-yl)-1-thia-3-azaspiro[4.5]deca-2,6,8-triene-7-carbonitrile (3ag):



The compound was prepared following the synthetic procedure A. The desired product was isolated by flash column chromatography (15:85 = EtOAc/Hexanes, v/v) to afford a yellow solid (31.6 mg, 72% yield). $[\alpha]_D^{20}$ = + 60.6 (c = 0.47, $CHCl_3$). **HPLC**: **73% ee**, (IB, IPA/n-hexane = 30/75, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 10.23 min (major), 15.56 min (minor). **mp**: 191-193 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.97 – 7.90 (m, 2H), 7.66 (dd, *J* = 8.2, 6.7 Hz, 1H), 7.49 – 7.44 (m, 4H), 7.43 – 7.38 (m, 3H), 7.12 (dd, *J* = 5.1, 1.3 Hz, 1H), 7.06 (dd, *J* = 3.6, 1.2 Hz, 1H), 6.86 (dd, *J* = 5.2, 3.5 Hz, 1H), 5.87 (d, *J* = 2.9 Hz, 1H), 5.19 (s, 2H), 4.94 (d, *J* = 2.9 Hz, 1H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)** δ 197.8, 191.3, 155.4, 137.6, 137.5, 137.3, 136.1, 131.6, 129.3, 129.1, 128.9, 128.7, 127.7, 126.7, 126.1, 121.6, 116.9, 83.6, 74.4, 46.1. **HRMS (ESI, m/z):** $[M + H]^+$ calculated for $C_{25}H_{18}N_3OS_2^+$: 440.0886; found: 440.0868

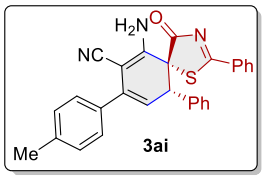
(5*R*,10*S*)-6-amino-2-(4-chlorophenyl)-4-oxo-8,10-diphenyl-1-thia-3-azaspiro[4.5]deca-2,6,8-triene-7-carbonitrile (3ah):



The compound was prepared following the synthetic procedure A. The desired product was isolated by flash column chromatography (15:85 = EtOAc/Hexanes, v/v) to afford a yellow semi-solid (31.8 mg, 68% yield). $[\alpha]_D^{20}$ = + 45.3 (c = 0.37, $CHCl_3$). **HPLC**: **96% ee**, (IC, IPA/n-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 22.98 min (major), 30.93 min (minor). **mp**: 197-199 °C. **^{1}H NMR (500 MHz,**

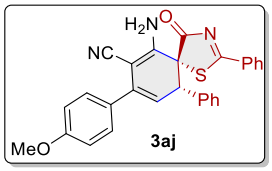
$CDCl_3$) δ 7.74 (d, *J* = 8.7 Hz, 2H), 7.47 – 7.41 (m, 4H), 7.40 – 7.35 (m, 4H), 7.35 – 7.31 (m, 2H), 7.18 (dd, *J* = 5.1, 2.0 Hz, 2H), 5.88 (d, *J* = 2.8 Hz, 1H), 5.29 (s, 2H), 4.58 (d, *J* = 2.8 Hz, 1H). **$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$)** δ 195.7, 191.3, 154.8, 142.6, 137.6, 137.4, 135.3, 130.2, 130.0, 129.7, 129.6, 128.74, 128.66, 128.6, 128.3, 127.6, 120.7, 117.1, 83.4, 74.6, 50.5. **HRMS (ESI, m/z):** $[M + H]^+$ calculated for $C_{27}H_{19}ClN_3OS^+$: 468.0932; found: 468.0922.

(5*R*,10*S*)-6-amino-4-oxo-2,10-diphenyl-8-(p-tolyl)-1-thia-3-azaspiro[4.5]deca-2,6,8-triene-7-carbonitrile (3ai):



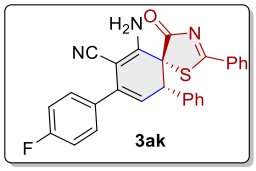
The compound was prepared following the synthetic procedure A. The desired product was isolated by flash column chromatography (15:85= EtOAc/Hexanes, v/v) to afford a yellow solid (34.8 mg, 78% yield). **$[\alpha]_D^{20}$** = + 44.0 (c = 0.40, $CHCl_3$). **HPLC**: **95% ee**, (IC, IPA/n-hexane = 70/30, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 23.41 min (major), 30.80 min (minor). **mp**: 195-197 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.81 (d, *J* = 7.9 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.44 – 7.32 (m, 6H), 7.25 – 7.14 (m, 5H), 5.85 (d, *J* = 3.0 Hz, 1H), 5.28 (s, 2H), 4.59 (d, *J* = 2.9 Hz, 1H), 2.39 (s, 3H). **$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$)** δ 197.2, 191.6, 155.0, 138.6, 137.2, 135.8, 135.6, 134.8, 131.4, 130.3, 129.3, 129.1, 128.8, 128.5, 128.3, 127.5, 120.1, 117.3, 83.5, 74.3, 50.4, 21.4. **HRMS (ESI, m/z):** $[M + H]^+$ calculated for $C_{28}H_{22}N_3OS^+$: 448.1479; found: 448.1479.

(5*R*,10*S*)-6-amino-8-(4-methoxyphenyl)-4-oxo-2,10-diphenyl-1-thia-3-azaspiro[4.5]deca-2,6,8-triene-7-carbonitrile (3aj):



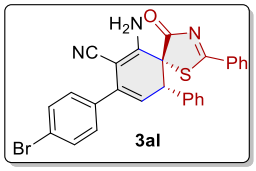
The compound was prepared following the synthetic procedure A. The desired product was isolated by flash column chromatography (20:80 = EtOAc/Hexanes, v/v) to afford a yellow solid (33.3mg, 72% yield). **$[\alpha]_D^{20}$** = + 46.4 (c = 0.37, $CHCl_3$). **HPLC**: **92% ee**, (IC, IPA/n-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 31.71 min (minor), 45.78 min (major). **mp**: 193-195 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.91 – 7.84 (m, 2H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.47 – 7.37 (m, 8H), 7.28 (s, 1H), 6.72 (d, *J* = 8.6 Hz, 2H), 5.87 (d, *J* = 3.1 Hz, 1H), 5.12 (s, 2H), 4.56 (d, *J* = 2.8 Hz, 1H), 3.68 (s, 3H). **$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$)** δ 197.3, 191.7, 159.6, 155.1, 137.7, 137.2, 135.9, 131.5, 131.4, 129.2, 129.0, 128.7, 127.7, 127.5, 121.5, 117.1, 113.7, 83.7, 74.5, 55.3, 49.6. **HRMS (ESI, m/z):** $[M + H]^+$ calculated for $C_{28}H_{22}N_3O_2S^+$: 464.1428; found: 464.1421

(5*R*,10*S*)-6-amino-8-(4-fluorophenyl)-4-oxo-2,10-diphenyl-1-thia-3-azaspiro[4.5]deca-2,6,8-triene-7-carbonitrile (3ak):



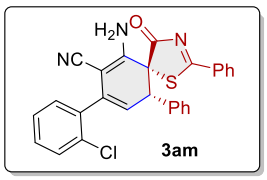
The compound was prepared following the synthetic procedure A. The desired product was isolated by flash column chromatography (8:92 = EtOAc/Hexanes, v/v) to afford a yellow solid (29.3 mg, 65% yield). **[α]**$_D^{20}$ = + 48.0 (c = 0.32, $CHCl_3$). **HPLC**: **95% ee**, (IC, IPA/n-hexane = 70/30, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 19.11 min (major), 25.01 min(minor). **mp**: 190-192 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.86 – 7.80 (m, 2H), 7.64 – 7.59 (m, 1H), 7.45 – 7.38 (m, 4H), 7.35 (dd, *J* = 7.6, 2.0 Hz, 2H), 7.22 – 7.16 (m, 3H), 7.10 (t, *J* = 8.6 Hz, 2H), 5.85 (d, *J* = 2.8 Hz, 1H), 5.19 (s, 2H), 4.59 (d, *J* = 2.8 Hz, 1H). **^{13}C{^{1}H } NMR (100 MHz, $CDCl_3$)** δ 197.1, 191.4, δ 163.13 (d, *J* = 247.9 Hz), 155.1, 136.4, 135.9, 135.4, 133.7, 130.3, 129.49 (d, *J* = 8.4 Hz), 129.2, 128.9, 128.6, 128.4, 120.8, 115.68 (d, *J* = 21.8 Hz), 83.5, 74.1, 50.4. **^{19}F{^{1}H } NMR (471 MHz, $CDCl_3$)** δ -112.9. **HRMS (ESI, m/z):** $[M + H]^+$ calculated for $C_{27}H_{19}FN_3OS^+$: 452.1228; found: 452.1229.

(5*R*,10*S*)-6-amino-8-(4-bromophenyl)-4-oxo-2,10-diphenyl-1-thia-3-azaspiro[4.5]deca-2,6,8-triene-7-carbonitrile (3al):



The compound was prepared following the synthetic procedure A. The desired product was isolated by flash column chromatography (15:85 = EtOAc/Hexanes, v/v) to afford a yellow solid (35.8 mg, 70% yield). **[α]**$_D^{20}$ = + 44.0 (c = 0.45, $CHCl_3$). **HPLC**: **93% ee**, (IB, IPA/n-hexane = 30/70, flow rate = 0.9 mL/min, λ = 254 nm), t_R = 22.57 min (major), 30.28 min (minor). **mp**: 199-201 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.91 – 7.80 (m, 2H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.43 (t, *J* = 7.9 Hz, 2H), 7.36 – 7.30 (m, 4H), 7.20 (dd, *J* = 5.1, 2.0 Hz, 3H), 5.89 (d, *J* = 2.8 Hz, 1H), 5.10 (s, 2H), 4.58 (d, *J* = 2.8 Hz, 1H). **^{13}C{^{1}H } NMR (125 MHz, $CDCl_3$)** δ 197.3, 191.2, 154.9, 137.8, 137.4, 137.1, 136.2, 134.6, 132.7, 132.0, 131.9, 131.5, 131.3, 129.4, 129.3, 129.1, 129.0, 128.8, 128.7, 127.6, 122.7, 120.0, 116.9, 83.6, 76.9, 74.0, 49.6. **HRMS (ESI, m/z):** $[M + H]^+$ calculated for $C_{27}H_{19}BrN_3OS^+$: 512.0427, 514.0407 found: 512.0419, 514.0400

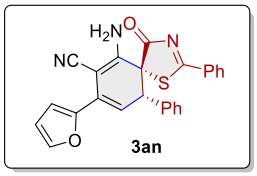
(5*R*,10*S*)-6-amino-8-(2-chlorophenyl)-4-oxo-2,10-diphenyl-1-thia-3-azaspiro[4.5]deca-2,6,8-triene-7-carbonitrile (3am):



The compound was prepared following the synthetic procedure A. The desired product was isolated by flash column chromatography (15:85 = EtOAc/Hexanes, v/v) to afford a yellow solid (37.4 mg, 80% yield). **[α]**$_D^{20}$ = + 61.3 (c = 0.67, $CHCl_3$). **HPLC**: **91% ee**, (IC, IPA/n-hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 22.88 min (minor), 32.44 min (major). **mp**: 191-193 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ

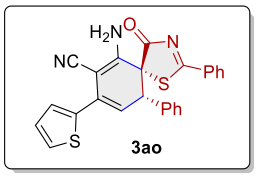
7.88 – 7.78 (m, 2H), 7.62 – 7.56 (m, 1H), 7.47 (dt, *J* = 7.4, 1.2 Hz, 1H), 7.43 – 7.36 (m, 2H), 7.37 – 7.28 (m, 5H), 7.23 – 7.11 (m, 3H), 5.77 (d, *J* = 2.7 Hz, 1H), 5.19 (s, 2H), 4.62 (d, *J* = 2.7 Hz, 1H). **^{13}C{^{1}H } NMR (125 MHz, CDCl$_3$)** δ 197.4, 191.6, 153.4, 137.0, 135.8, 135.3, 133.5, 131.5, 130.9, 130.3, 130.0, 129.9, 129.1, 128.9, 128.5, 128.3, 127.1, 122.3, 116.4, 84.8, 74.2, 50.1 **HRMS (ESI, m/z):** $[M + H]^+$ calculated for $C_{27}H_{19}ClN_3OS^+$: 468.0932; found: 468.0941

(5*R*,10*S*)-6-amino-8-(furan-2-yl)-4-oxo-2,10-diphenyl-1-thia-3-azaspiro[4.5]deca-2,6,8-triene-7-carbonitrile (3an):



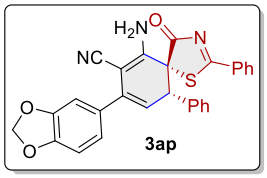
The compound was prepared following the synthetic procedure A. The desired product was isolated by flash column chromatography (8:92 = EtOAc/Hexanes, v/v) to afford a yellow solid (33.0 mg, 78% yield). **[α]**$_D^{20}$ = + 44.5 (c = 0.40, $CHCl_3$). **HPLC**: **74% ee**, (ID, IPA/n-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 18.50 min (minor), 24.03 min (major). **mp**: 197-199 °C. **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.84 – 7.74 (m, 2H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.44 – 7.31 (m, 5H), 7.24 – 7.14 (m, 3H), 6.89 (d, *J* = 3.5 Hz, 1H), 6.47 (dd, *J* = 3.5, 1.8 Hz, 1H), 6.25 (d, *J* = 3.1 Hz, 1H), 5.31 (s, 2H), 4.58 (d, *J* = 3.1 Hz, 1H). **^{13}C{^{1}H } NMR (100 MHz, CDCl$_3$)** δ 197.3, 191.3, 155.6, 149.9, 142.6, 135.9, 135.3, 131.3, 130.3, 129.2, 128.8, 128.5, 128.3, 126.1, 117.7, 117.4, 111.7, 108.5, 80.0, 73.9, 49.9. **HRMS (ESI, m/z):** $[M + H]^+$ calculated for $C_{25}H_{18}N_3O_2S^+$: 424.1115 found: 424.1115.

(5*R*,10*S*)-6-amino-4-oxo-2,10-diphenyl-8-(thiophen-2-yl)-1-thia-3-azaspiro[4.5]deca-2,6,8-triene-7-carbonitrile (3ao):



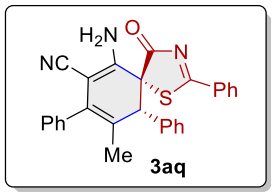
The compound was prepared following the synthetic procedure A. The desired product was isolated by flash column chromatography (8:92 = EtOAc/Hexanes, v/v) to afford a yellow solid (31.6 mg, 72% yield). **[α]**$_D^{20}$ = + 52.8 (c = 0.5, $CHCl_3$). **HPLC**: **80% ee**, (IC, IPA/n-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 20.78 min (minor), 28.16 min (major). **mp**: 197-199 °C. **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.84 – 7.78 (m, 2H), 7.60 (t, *J* = 7.5 Hz, 1H), 7.40 (d, *J* = 8.0 Hz, 2H), 7.39 – 7.33 (m, 3H), 7.27 (d, *J* = 5.9 Hz, 1H), 7.23 – 7.16 (m, 3H), 7.08 (dd, *J* = 5.4, 3.7 Hz, 1H), 6.00 (d, *J* = 3.1 Hz, 1H), 5.34 (s, 2H), 4.58 (d, *J* = 3.1 Hz, 1H). **^{13}C{^{1}H } NMR (100 MHz, CDCl$_3$)** δ 197.2, 191.2, 155.6, 139.8, 135.9, 135.2, 131.3, 130.3, 130.2, 129.2, 128.9, 128.6, 128.3, 127.9, 126.2, 125.5, 120.2, 117.2, 82.5, 73.9, 50.2. **HRMS (ESI, m/z):** $[M + H]^+$ calculated for $C_{25}H_{18}N_3OS_2^+$: 440.0886 found: 440.0887.

(5*R*,10*S*)-6-amino-8-(benzo[d][1,3]dioxol-5-yl)-4-oxo-2,10-diphenyl-1-thia-3-azaspiro[4.5]deca-2,6,8-triene-7-carbonitrile (3ap):



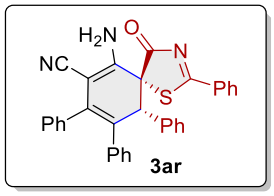
The compound was prepared following the synthetic procedure A. The desired product was isolated by flash column chromatography (20:80 = EtOAc/Hexanes, v/v) to afford a yellow solid (33.4 mg, 70% yield). **[α]**$_D^{20}$ = + 49.7 (c = 0.45, $CHCl_3$). **HPLC**: **80% ee**, (IC, IPA/n-hexane = 30/70, flow rate = 1 mL/min, λ = 254 nm), t_R = 34.76 min (minor), 52.22 min (major). **mp**: 195-197 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.86 – 7.81 (m, 2H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 2H), 7.38 – 7.31 (m, 2H), 7.19 (dd, *J* = 5.0, 2.1 Hz, 3H), 6.96 – 6.90 (m, 2H), 6.84 (d, *J* = 8.0 Hz, 1H), 6.00 (d, *J* = 1.6 Hz, 2H), 5.82 (d, *J* = 2.9 Hz, 1H), 5.12 (s, 2H), 4.57 (d, *J* = 2.9 Hz, 1H). **^{13}C{^{1}H } NMR (100 MHz, $CDCl_3$)** δ 197.2, 191.5, 154.9, 148.2, 147.9, 137.0, 135.9, 135.5, 131.8, 131.5, 130.3, 129.2, 128.9, 128.5, 128.3, 121.5, 120.2, 117.1, 108.5, 108.3, 101.5, 83.9, 74.3, 50.3. **HRMS (ESI, m/z):** $[M + H]^+$ calculated for $C_{28}H_{20}N_3O_3S^+$: 478.1220 found: 478.1216.

(5*R*,10*R*)-6-amino-9-methyl-4-oxo-2,8,10-triphenyl-1-thia-3-azaspiro[4.5]deca-2,6,8-triene-7-carbonitrile (3aq):



The compound was prepared following the synthetic procedure A. The desired product was isolated by flash column chromatography (15:85 = EtOAc/Hexanes, v/v) to afford a yellow solid (31.3 mg,70% yield). **[α]**$_D^{20}$ = - 71.6 (c = 0.65, $CHCl_3$). **HPLC**: **74% ee** (IC, IPA/n-hexane = 30/70, flow rate = 1.0 mL/min, l = 254 nm), t_R = 18.76 min (minor), 43.86 min (major). **mp**: 191-193°C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.99 (d, *J* = 7.5 Hz, 2H), 7.68 (t, *J* = 7.5 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 2H), 7.44 – 7.33 (m, 6H), 7.30 (d, *J* = 7.7 Hz, 2H), 7.25 (d, *J* = 3.6 Hz, 2H), 4.94 (s, 2H), 4.07 (s, 1H), 1.51 (s, 3H). **^{13}C{^{1}H } NMR (100 MHz, $CDCl_3$)** δ 194.9, 189.7, 150.8, 138.2, 136.9, 135.9, 131.6, 130.0, 129.9, 129.4, 129.3, 129.1, 129.0, 128.6, 127.9, 125.6, 124.8, 117.6, 86.0, 73.2, 55.0, 19.1. **HRMS (ESI, m/z):** $[M + H]^+$ calculated for $C_{28}H_{22}N_3OS^+$: 448.1479 found: 448.1475.

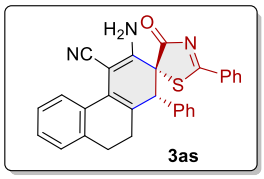
(5*R*,10*R*)-6-amino-4-oxo-2,8,9,10-tetraphenyl-1-thia-3-azaspiro[4.5]deca-2,6,8-triene-7-carbonitrile (3ar):



The compound was prepared following the synthetic procedure A. The desired product was isolated by flash column chromatography (15:85 = EtOAc/Hexanes, v/v) to afford a yellow solid (39.8 mg,78% yield).

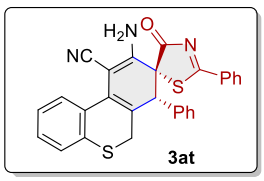
[α]$_D^{20}$ = -72.0 (c = 0.57, $CHCl_3$). **HPLC**: **66% ee** (IC, IPA/n-hexane = 30/70, flow rate = 1.0 mL/min, l = 254 nm), t_R = 14.63 min (minor), 32.38 min (major). **mp**: 199-201 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.00 (d, *J* = 7.7 Hz, 2H), 7.68 (t, *J* = 7.5 Hz, 1H), 7.49 (t, *J* = 7.8 Hz, 2H), 7.25 (d, *J* = 1.9 Hz, 2H), 7.19 (d, *J* = 4.6 Hz, 4H), 7.16 (t, *J* = 5.2 Hz, 4H), 6.90 (t, *J* = 3.0 Hz, 3H), 6.72 – 6.61 (m, 2H), 5.18 (s, 2H), 4.43 (s, 1H). **^{13}C{^{1}H } NMR (125 MHz, $CDCl_3$)** δ 194.2, 188.9, 152.4, 139.5, 137.9, 136.9, 136.0, 132.4, 131.5, 130.5, 130.2, 129.7, 129.3, 129.1, 129.0, 128.4, 128.3, 128.1, 127.7, 127.6, 126.3, 117.6, 86.1, 73.4, 55.0. **HRMS (ESI, m/z):** $[M + H]^+$ calculated for $C_{33}H_{24}N_3OS^+$: 510.1635 found: 510.1635.

(1*R*,2*R*)-3-amino-4'-oxo-1,2'-diphenyl-9,10-dihydro-1H,4'H-spiro[phenanthrene-2,5'-thiazole]-4-carbonitrile (3as):



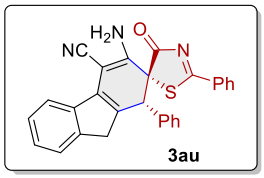
The compound was prepared following the synthetic procedure A. The desired product was isolated by flash column chromatography (15:85 = EtOAc/Hexanes, v/v) to afford a yellow solid (36.7 mg,80% yield). **[α]**$_D^{20}$ = + 42.5 (c = 0.47, $CHCl_3$). **HPLC**: **81% ee** (IC, IPA/n-hexane = 30/70, flow rate = 1.0 mL/min, l = 254 nm), t_R = 21.04 min (minor), 41.82 min (major). **mp**: 201-203 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.90 – 7.82 (m, 2H), 7.73 – 7.59 (m, 2H), 7.43 (t, *J* = 7.8 Hz, 2H), 7.36 – 7.26 (m, 3H), 7.25 – 7.15 (m, 5H), 5.11 (s, 2H), 4.57 (d, *J* = 3.1 Hz, 1H), 2.73 – 2.56 (m, 2H), 2.28 (dddd, *J* = 17.7, 14.4, 6.1, 3.5 Hz, 1H), 1.98 – 1.86 (m, 1H). **^{13}C{^{1}H } NMR (100 MHz, $CDCl_3$)** δ 196.7, 190.7, 154.0, 136.7, 135.9, 133.6, 132.2, 131.5, 130.8, 130.5, 129.2, 128.9, 128.7, 128.3, 127.7, 127.5, 127.2, 126.7, 124.6, 117.9, 81.8, 73.6, 54.5, 29.1, 27.3. **HRMS (ESI, m/z):** $[M + H]^+$ calculated for $C_{29}H_{22}N_3OS^+$: 460.1479 found: 460.1479.

(7*R*,8*R*)-9-amino-4'-oxo-2',7-diphenyl-4'H,6H,7H-spiro[benzo[c]thiochromene-8,5'-thiazole]-10-carbonitrile (3at):



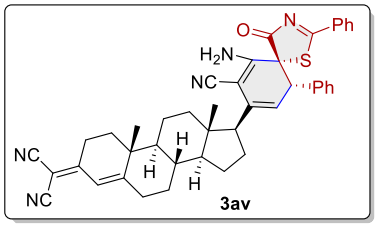
The compound was prepared following the synthetic procedure A. The desired product was isolated by flash column chromatography (20:80 = EtOAc/Hexanes, v/v) to afford a yellow solid (39.2 mg, 82% yield). **[α]**$_D^{20}$ = + 77.7 (c = 0.60, $CHCl_3$). **HPLC**: **69% ee** (IC, IPA/n-hexane = 30/70, flow rate = 1.0 mL/min, l = 254 nm), t_R = 24.18 min (minor), 37.83 min (major). **mp**: 200-201 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.86 (d, *J* = 7.7 Hz, 2H), 7.64 (dd, *J* = 10.9, 7.4 Hz, 2H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.38 (d, *J* = 7.6 Hz, 1H), 7.31 – 7.26 (m, 3H), 7.24 – 7.16 (m, 4H), 5.28 (s, 2H), 4.70 (d, *J* = 3.0 Hz, 1H), 3.45 (dd, *J* = 15.8, 3.1 Hz, 1H), 2.82 (d, *J* = 15.8 Hz, 1H). **^{13}C{^{1}H } NMR (100 MHz, $CDCl_3$)** δ 196.4, 190.3, 154.6, 136.0, 134.0, 132.8, 132.0, 131.3, 130.8, 129.4, 129.3, 129.0, 128.9, 128.6, 128.4, 128.3, 126.9, 126.1, 126.0, 117.6, 82.1, 73.1, 54.1, 28.8. **HRMS (ESI, m/z):** $[M + H]^+$ calculated for $C_{28}H_{20}N_3OS_2^+$: 478.1043 found: 478.1035.

(1*R*,2*R*)-3-amino-4'-oxo-1,2'-diphenyl-1,9-dihydro-4'H-spiro[fluorene-2,5'-thiazole]-4-carbonitrile (3au):



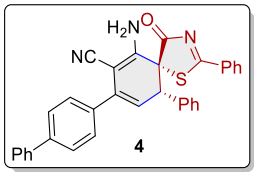
The compound was prepared following the synthetic procedure A. The desired product was isolated by flash column chromatography (15:85 = EtOAc/Hexanes, v/v) to afford a yellow solid (30.3 mg, 68% yield). **[α]**$_D^{20}$ = + 74.1 (c = 0.57, $CHCl_3$). **HPLC**: **84% ee** (IC, IPA/n-hexane = 30/70, flow rate = 1.0 mL/min, l = 254 nm), t_R = 14.96 min (minor), 28.95 min (major). **mp**: 198-200 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.01 (d, *J* = 7.7 Hz, 1H), 7.85 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.65 – 7.60 (m, 1H), 7.46 – 7.34 (m, 7H), 7.25 – 7.22 (m, 3H), 5.06 (s, 2H), 4.76 (d, *J* = 2.1 Hz, 1H), 3.59 (dd, *J* = 24.0, 2.1 Hz, 1H), 3.10 (dd, *J* = 24.1, 2.2 Hz, 1H). **^{13}C{^{1}H } NMR (125 MHz, $CDCl_3$)** δ 197.1, 190.9, 154.0, 143.4, 140.7, 135.9, 134.2, 133.8, 132.8, 131.4, 130.8, 130.7, 129.4, 129.2, 129.0, 128.9, 128.8, 128.3, 126.9, 125.6, 123.9, 119.7, 116.9, 79.6, 75.0, 51.9, 38.8. **HRMS (ESI, m/z):** [M + H]$^+$ calculated for $C_{28}H_{20}N_3OS^+$: 446.1322 found 446.1333.

2-((8*S*,9*S*,10*R*,13*S*,14*S*,17*S*)-17-((5*R*,10*S*)-6-amino-7-cyano-4-oxo-2,10-diphenyl-1-thia-3-azaspiro [4.5]deca-2,6,8-trien-8-yl)-10,13-dimethyl-1,2,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-3H-cyclopenta[a]phenanthren-3-ylidene)malononitrile (3av):



The compound was prepared following the synthetic procedure A. The desired product was isolated by flash column chromatography (20:80 = EtOAc/Hexanes, v/v) to afford a yellow solid (45.9 mg, 68% yield). **[α]**$_D^{20}$ = + 55.2 (c = 0.50, $CHCl_3$). **mp**: 199-201 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.80 (d, *J* = 7.8 Hz, 2H), 7.58 (d, *J* = 7.5 Hz, 1H), 7.39 (t, *J* = 7.7 Hz, 2H), 7.31 – 7.26 (m, 2H), 7.19 (dd, *J* = 10.4, 5.0 Hz, 3H), 6.47 (s, 1H), 5.62 (d, *J* = 2.5 Hz, 1H), 5.06 (s, 2H), 4.41 (s, 1H), 2.92 (dt, *J* = 17.4, 3.8 Hz, 1H), 2.71 – 2.35 (m, 4H), 2.02 – 1.87 (m, 2H), 1.86 – 1.74 (m, 3H), 1.73 – 1.66 (m, 1H), 1.66 – 1.52 (m, 3H), 1.47 (td, *J* = 13.9, 13.4, 3.7 Hz, 2H), 1.31 (t, *J* = 8.1 Hz, 2H), 1.17 (s, 3H), 1.12 – 0.96 (m, 2H), 0.81 (s, 3H). **^{13}C{^{1}H } NMR (100 MHz, $CDCl_3$)** δ 196.8, 191.5, 171.2, 170.2, 153.4, 135.8, 134.2, 131.4, 130.2, 129.1, 128.8, 128.4, 128.2, 119.4, 119.0, 117.7, 113.3, 112.5, 86.4, 74.9, 55.4, 53.8, 53.1, 50.1, 43.7, 39.3, 37.8, 36.4, 34.6, 33.8, 32.2, 26.3, 25.3, 24.1, 21.3, 17.7, 13.7. **HRMS (ESI, m/z):** [M + H]$^+$ calculated for $C_{43}H_{42}N_5OS^+$: 676.3105 found: 676.3103.

(5R,10S)-8-([1,1'-biphenyl]-4-yl)-6-amino-4-oxo-2,10-diphenyl-1-thia-3-azaspiro[4.5]deca-2,6,8-triene-7-carbonitrile (4):



To a stirred solution of **3am** (51.1 mg, 0.1 mmol, 1.0 equiv), in THF (2 ml), $Pd(PPh_3)_4$ (11.5 mg, 0.01 mmol, 10 mol %), phenylboronic acid (18.3 mg, 0.15 mmol, 1.5 equiv) and K_2CO_3 (27.6 mg, 0.2 mmol, 2.0 equiv) were added. The reaction mixture was stirred at 70 °C for 12 h. After the reaction was completed (monitored by TLC), the resulting mixture was concentrated under reduced pressure, and the residue was purified by column chromatography on silica gel to give the product **4** (30.5 mg, 60% yield). **$[\alpha]_D^{20}$** = + 71.3 (c = 0.62, $CHCl_3$**) HPLC**: **94% ee** (IC, IPA/n-hexane = 30/70, flow rate = 1.0 mL/min, l = 254 nm), t_R = 25.48 min (minor), 37.78 min (major). **mp**: 197-199 °C **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.84 (d, *J* = 7.7 Hz, 2H), 7.64 (t, *J* = 8.2 Hz, 5H), 7.55 (d, *J* = 8.2 Hz, 2H), 7.49 – 7.40 (m, 4H), 7.38 (dd, *J* = 7.1, 3.2 Hz, 3H), 7.20 (d, *J* = 5.7 Hz, 3H), 5.96 (d, *J* = 2.9 Hz, 1H), 5.29 (s, 2H), 4.63 (d, *J* = 2.9 Hz, 1H). **^{13}C{^{1}H } NMR (100 MHz, $CDCl_3$)** δ 197.2, 191.5, 155.2, 141.6, 140.6, 136.9, 136.5, 135.9, 135.5, 131.4, 130.3, 129.2, 129.0, 128.9, 128.6, 128.4, 128.1, 127.6, 127.4, 127.2, 120.9, 117.2, 83.4, 74.2, 50.4. **HRMS (ESI, m/z):** $[M + H]^+$ calculated for $C_{23}H_{24}N_3OS^+$: 510.1635 found: 510.1634.

X-ray crystallographic figures and data of 3aa

A suitable single crystal of **3aa** was grown by slow evaporation of a solution of **3aa** compound in a mixture of solvent (Ethyl acetate/hexane=1:1) at room temperature.

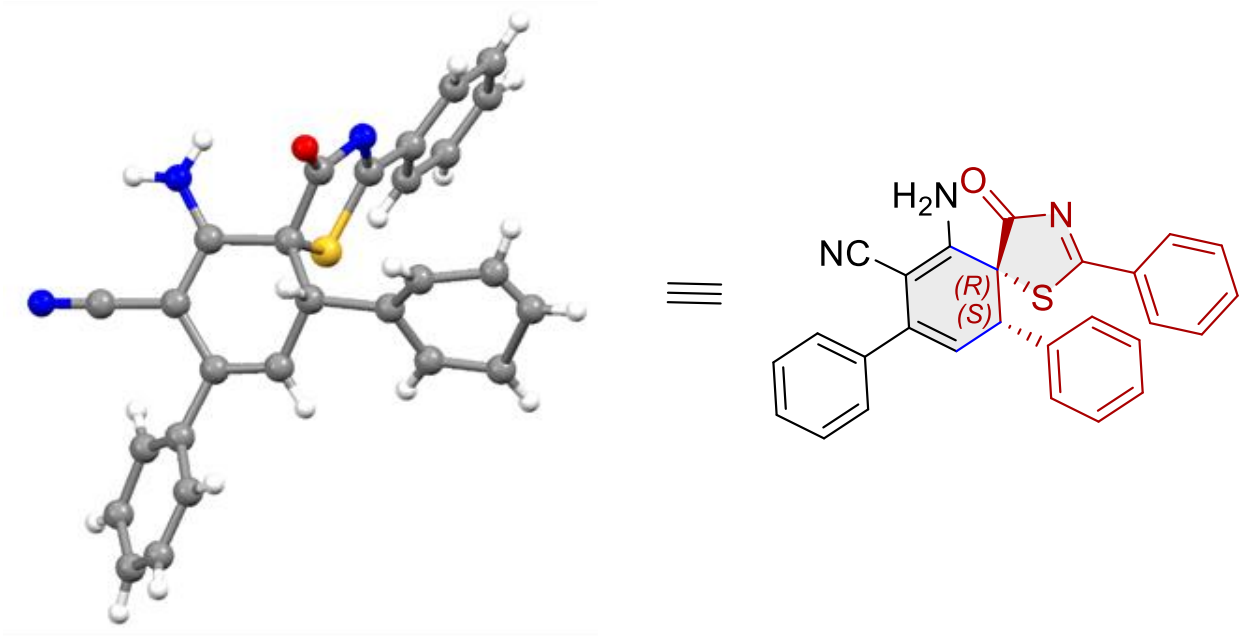


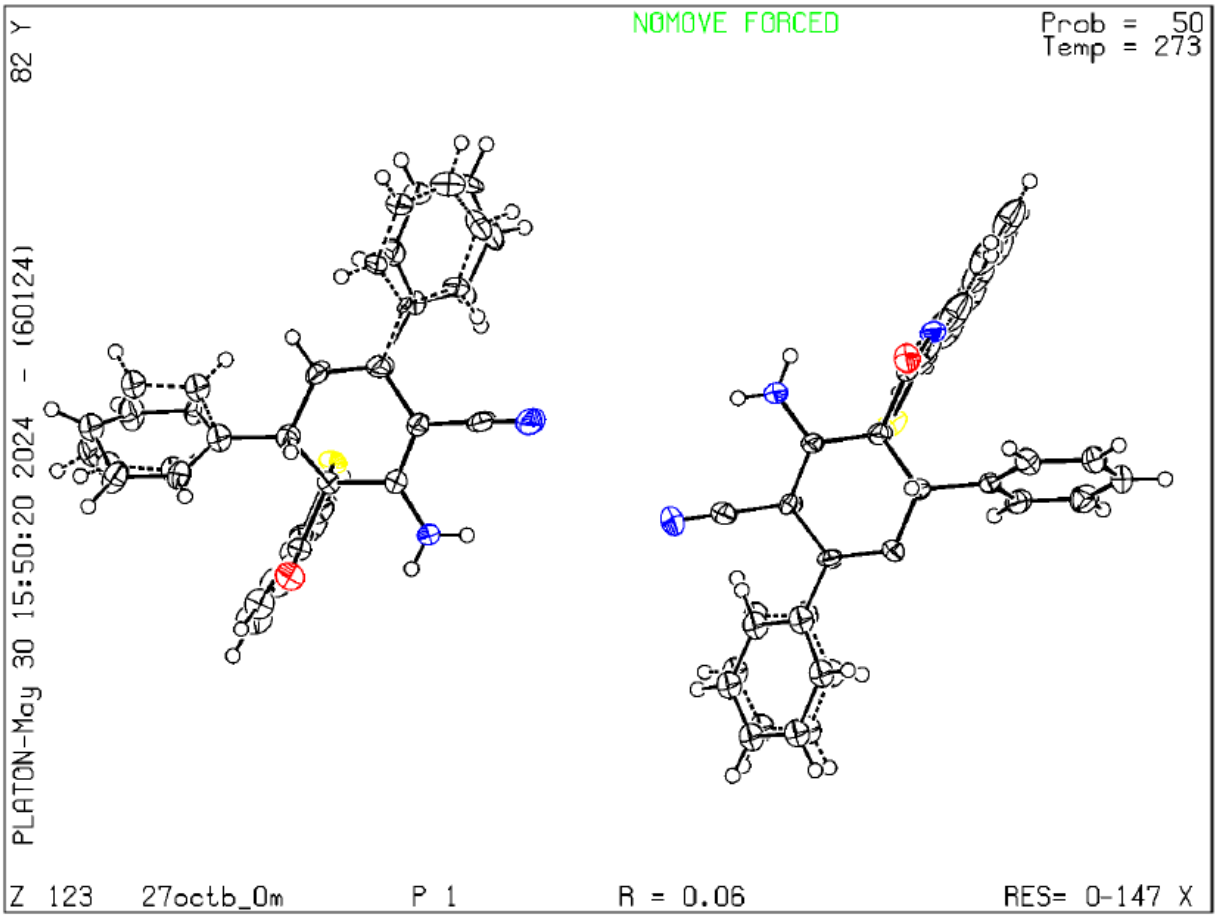
Figure S1: Crystal structure (with 50% ellipsoid probability) of **3aa** (CCDC No. 2359432)

(Note: Asymmetric unit is represented; thermal splitting has been removed for clarity)

Table S8: Crystal data and structure refinement for 3aa (CCDC No. 2359432)

Table 1 Crystal data and structure refinement for 27octb_0m.

Identification code	27octb_0m
Empirical formula	$C_{62}H_{53}N_6O_6S_2$
Formula weight	1042.22
Temperature/K	273.15
Crystal system	triclinic
Space group	P1
a/Å	10.2217(3)
b/Å	11.1542(3)
c/Å	13.1904(4)
α/°	95.1110(10)
β/°	94.0180(10)
γ/°	111.2480(10)
Volume/Å^3	1387.58(7)
Z	1
ρ_{calc}g/cm^3	1.247
μ/mm^{-1}	0.153
F(000)	547.0
Crystal size/mm^3	0.2 × 0.2 × 0.2
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.836 to 56.68
Index ranges	$-13 \leq h \leq 13$, $-14 \leq k \leq 14$, $-17 \leq l \leq 17$
Reflections collected	22503
Independent reflections	13648 [R_{int} = 0.0263, R_{sigma} = 0.0515]
Data/restraints/parameters	13648/71/648
Goodness-of-fit on F^2	1.028
Final R indexes [I>=2σ (I)]	R_1 = 0.0517, wR_2 = 0.1256
Final R indexes [all data]	R_1 = 0.0577, wR_2 = 0.1310
Largest diff. peak/hole / e Å^{-3}	0.35/-0.61
Flack parameter	0.13(3)


NOMOVE FORCED
Prob = 50
Temp = 273
82 Y
PLATON-May 30 15:50:20 2024 - (60124)
Z 123 27octb_0m P 1 R = 0.06 RES= 0-147 X

Quantum yield calculation:

Calculated quantum yield (ϕ) for compound **3aa** = 5.89%.

Here, we used quinine sulfate as the internal standard with ϕ = 54.6% in 0.5 M H_2SO_4. Using formula:

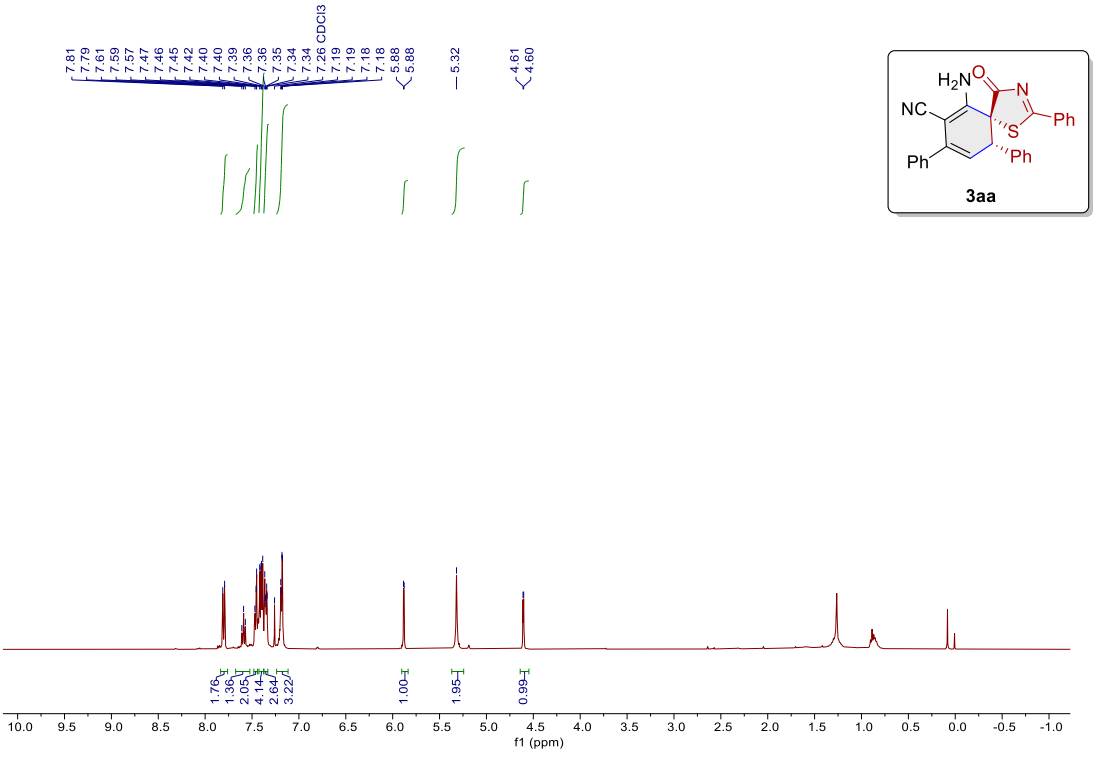
$$\phi_X = \left(\frac{A_R}{A_X}\right)\left(\frac{E_X}{E_R}\right)\left(\frac{\eta_X}{\eta_R}\right)^2 \phi_R$$

Here, the absorbance was set to 0.2 at λ= 350 nm for both the sample and internal standard, E_X is the area under the curve for the sample **(3aa)**, and E_R is the area under the curve for quinine sulfate (internal standard). η_X is the refractive index for methanol, and η_R is the refractive index for H_2O. ϕ_R is the quantum yield for quinine sulfate.

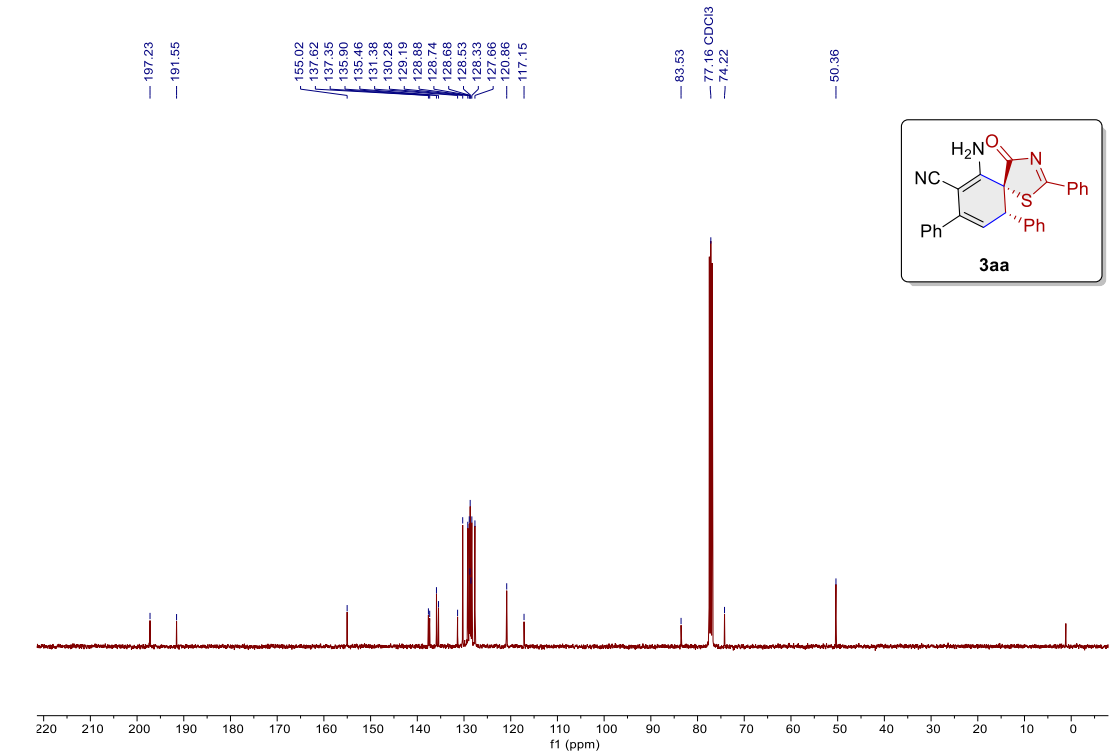
References:

1. (a) Zhu, X.-L.; He, W.-J.; Yu, L.-L.; Cai, C.-W.; Zuo, Z.-L.; Qin, D.-B.; Liu, Q.-Z.; Jing, L.-H. Organocatalytic Asymmetric Vinylogous Michael Addition of Dicyanoolefins to Imine Intermediates Generated *in situ* from Arenesulfonylalkylindoles. *Adv. Synth. Catal.* **2012**, *354*, 2965-2970. (b) Dhara, H. N.; Rakshit, A.; Alam, T.; Sahoo, A. K.; Patel, B. K. Visible-Light-Mediated Solvent-Switched Photosensitizer-Free Synthesis of Polyfunctionalized Quinolines and Pyridines. *Org. Lett.* **2023**, *25*, 471-476.
2. (a) Lin, L.; Yang, Y.; Wang, M.; Lai, L.; Guo, Y.; Wang, R. Oxidative *N*-Heterocyclic Carbene Catalyzed Stereoselective Annulation of Simple Aldehydes and 5-Alkenyl Thiazolones *Chem. Commun.* **2015**, *51*, 8134-8137. (b) Manna, A.; Rohilla, S.; Singh, V. K. Enantioselective Synthesis of Thiazolopyran Derivatives via a Direct Vinylogous Michael–*oxa*-Michael Sequence. *Org. Lett.* **2024**, *26*, 280-285.

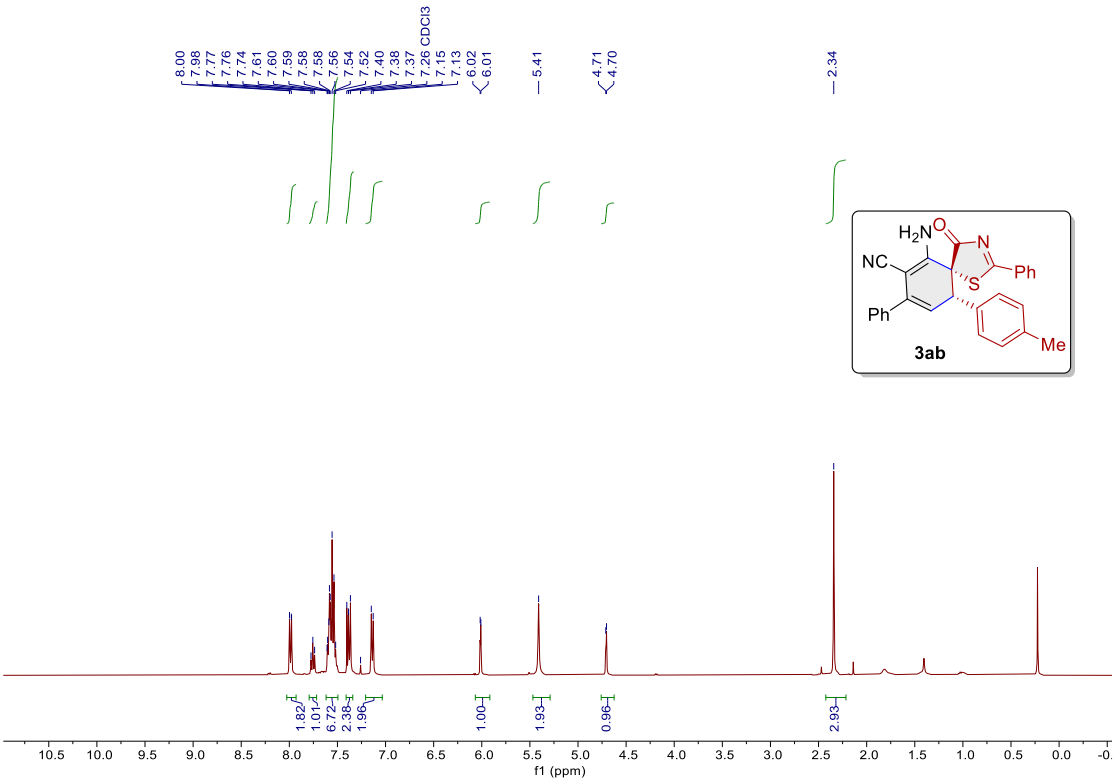
NMR Spectra:



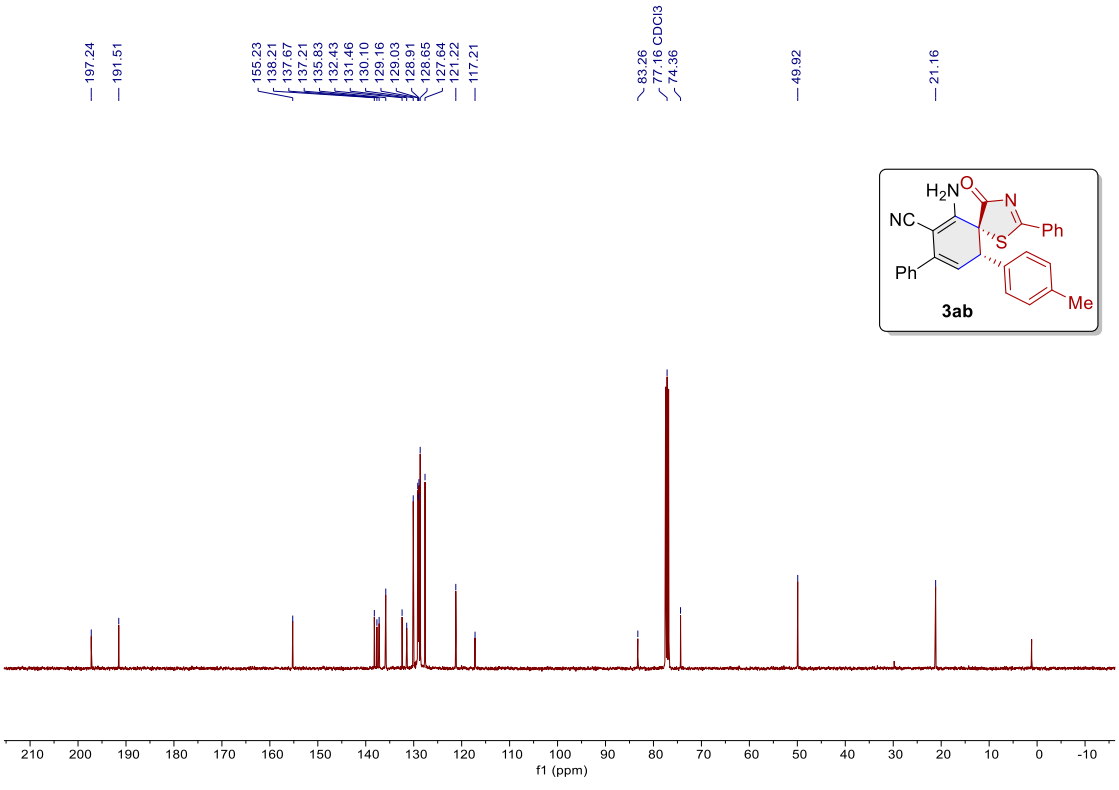
400 MHz ^{1}H NMR spectra of compound **3aa** in $CDCl_3$



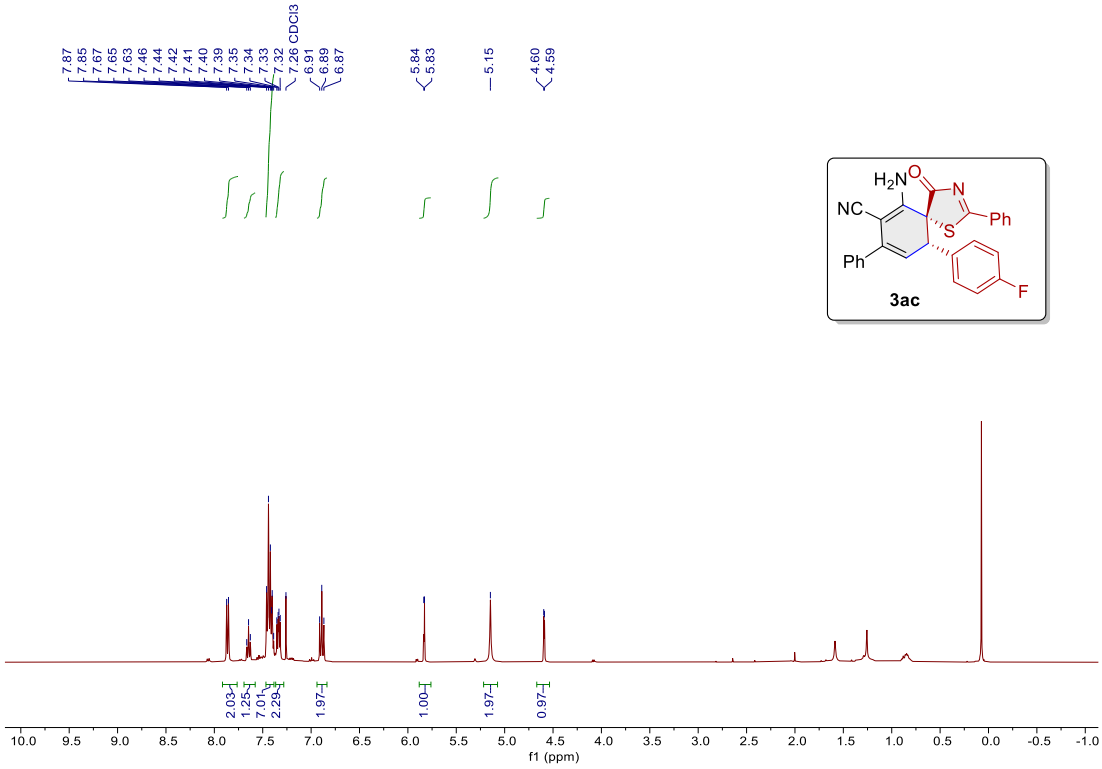
100 MHz $^{13}C\{^{1}H\}$ NMR spectra of compound **3aa** in $CDCl_3$



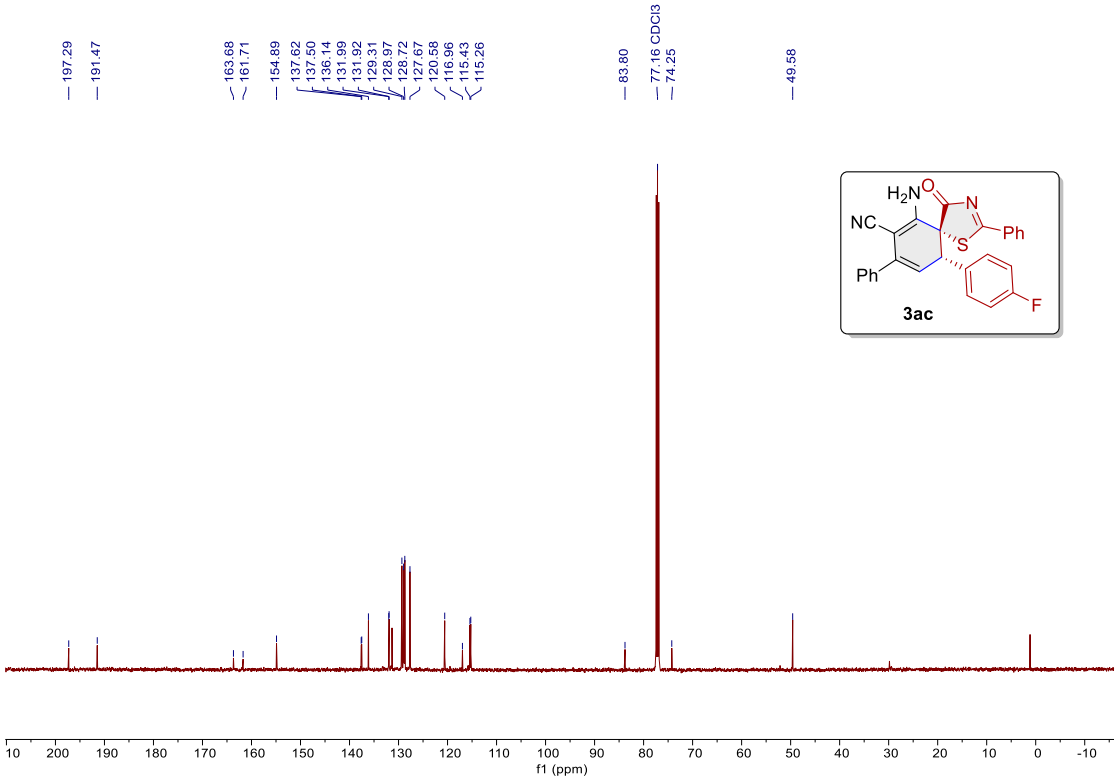
400 MHz ^{1}H NMR spectra of compound **3ab** in $CDCl_3$



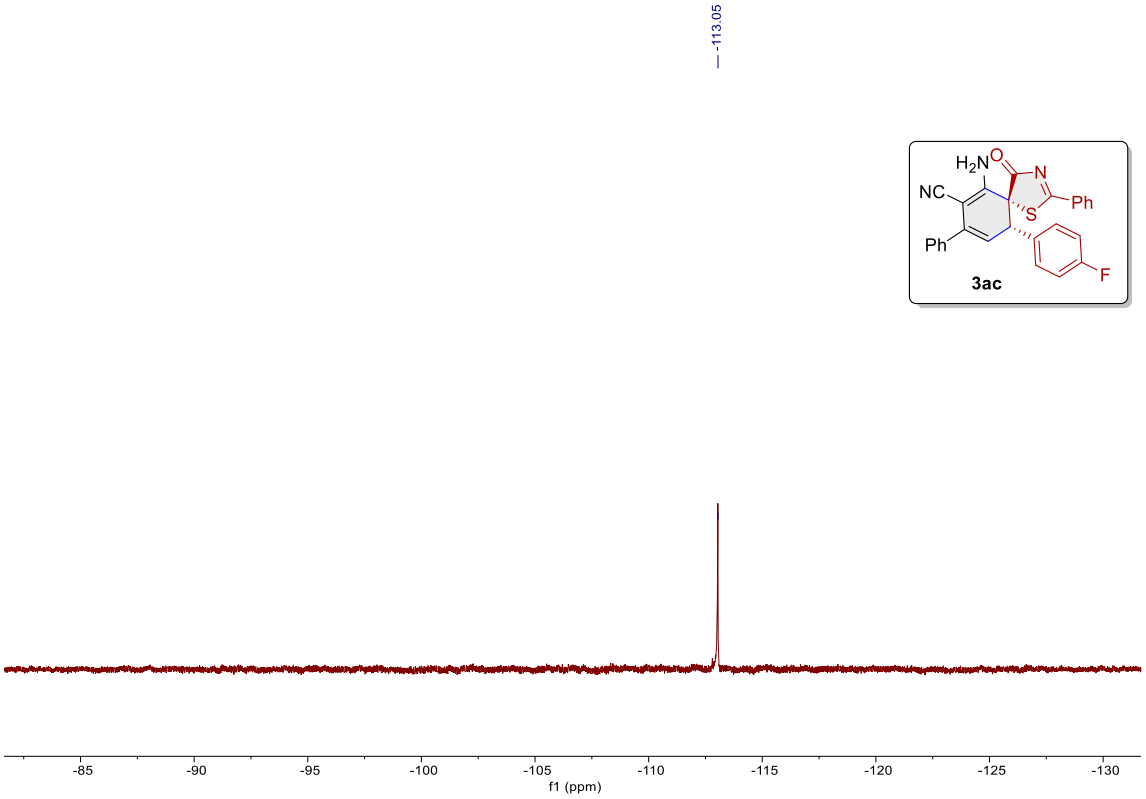
100 MHz $^{13}C\{^{1}H\}$ NMR spectra of compound **3ab** in $CDCl_3$



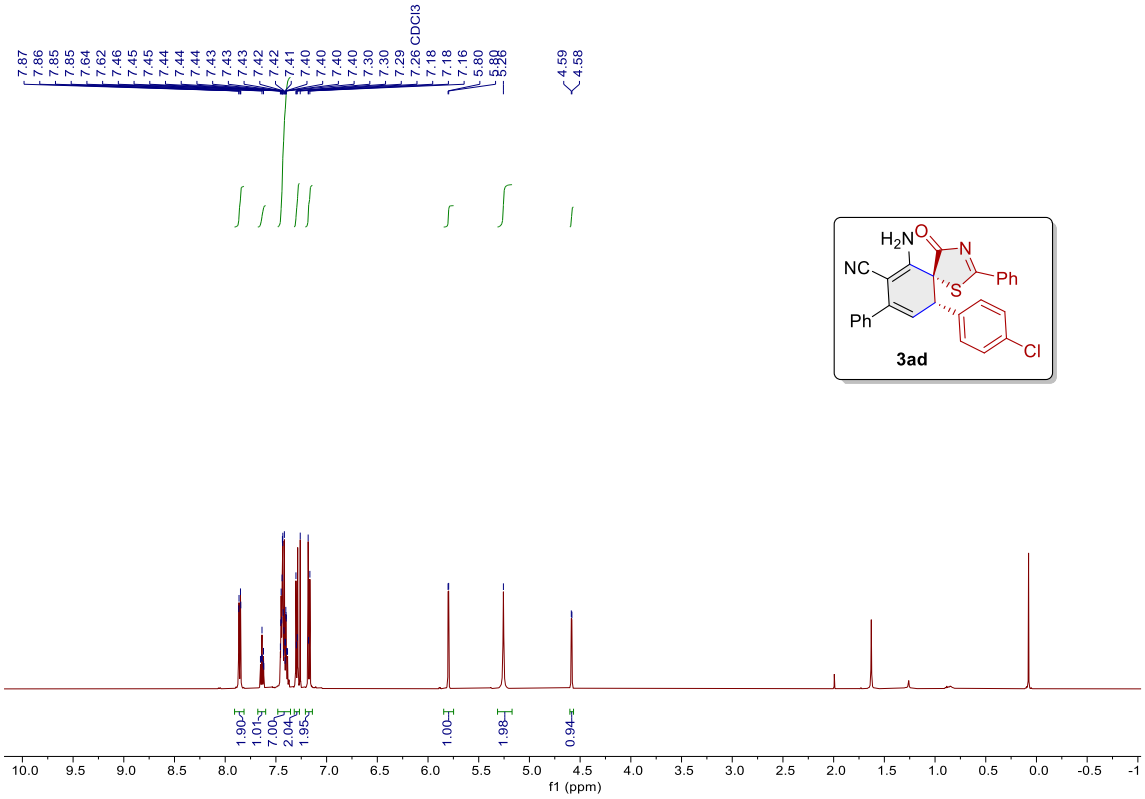
400 MHz ^{1}H NMR spectra of compound **3ac** in $CDCl_3$



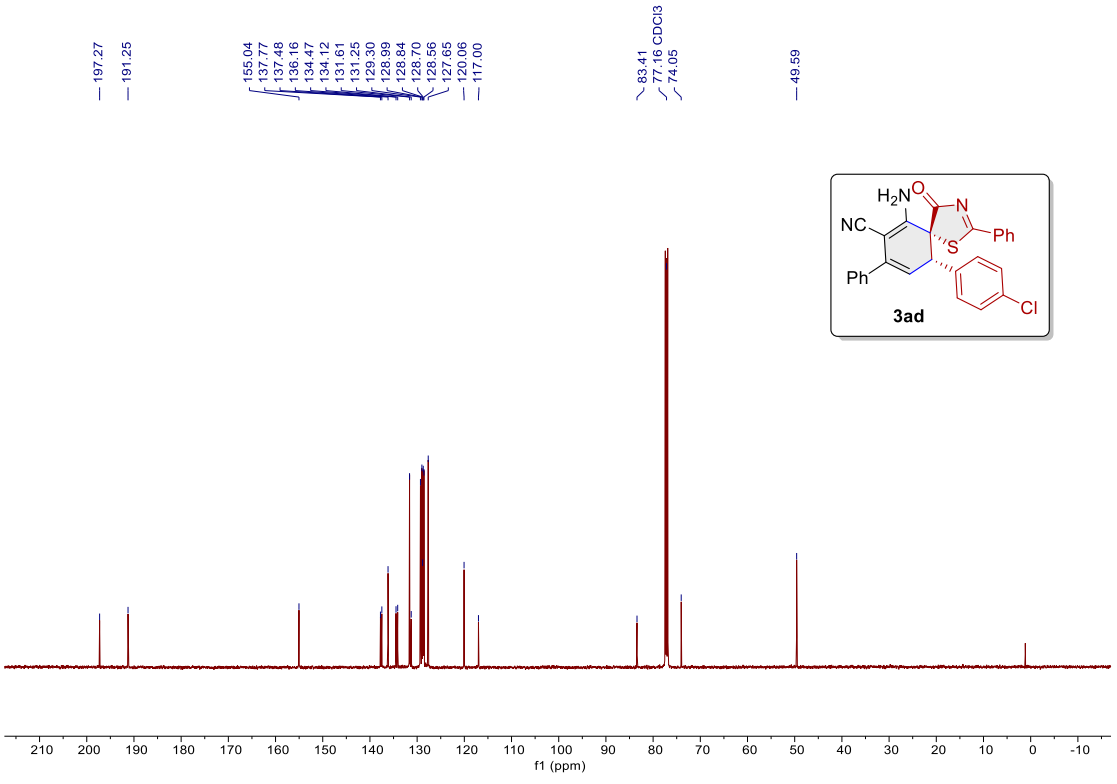
100 MHz ^{13}C{^{1}H} NMR spectra of compound **3ac** in $CDCl_3$



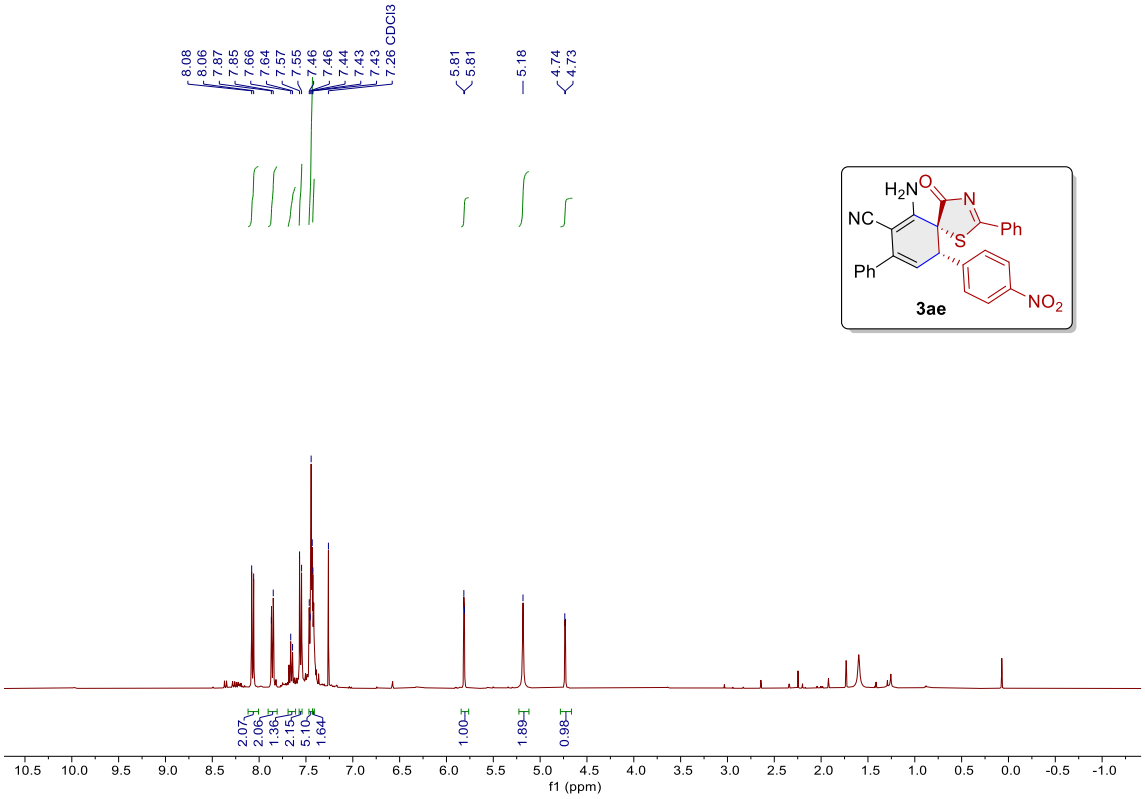
471 MHz $^{19}F\{^{1}H\}$ NMR spectra of compound **3ac** in $CDCl_3$



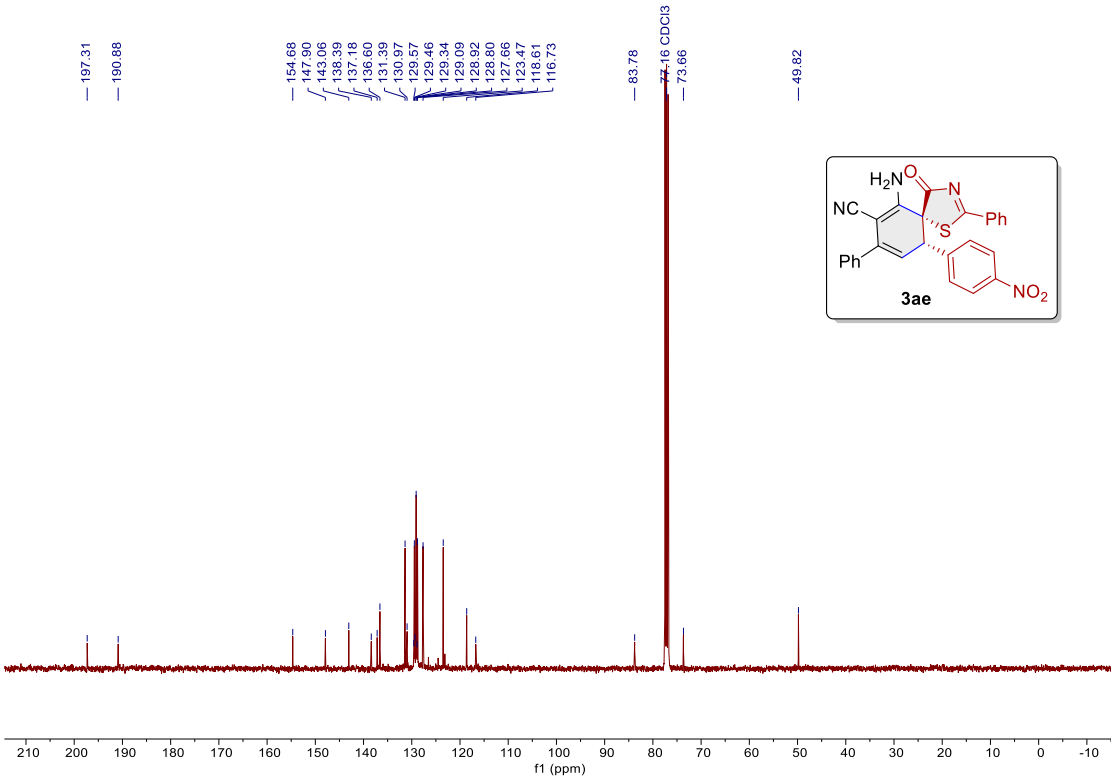
500 MHz ^{1}H NMR spectra of compound **3ad** in $CDCl_3$



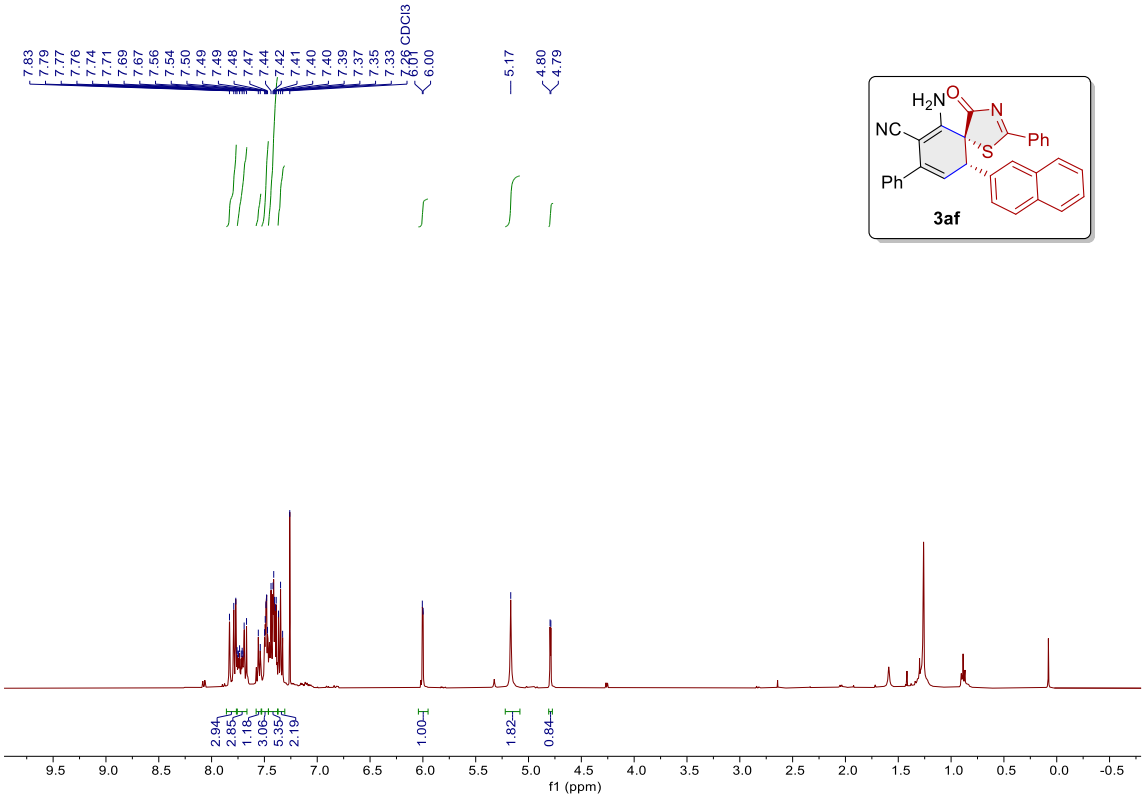
125 MHz ^{13}C{^{1}H} NMR spectra of compound **3ad** in $CDCl_3$



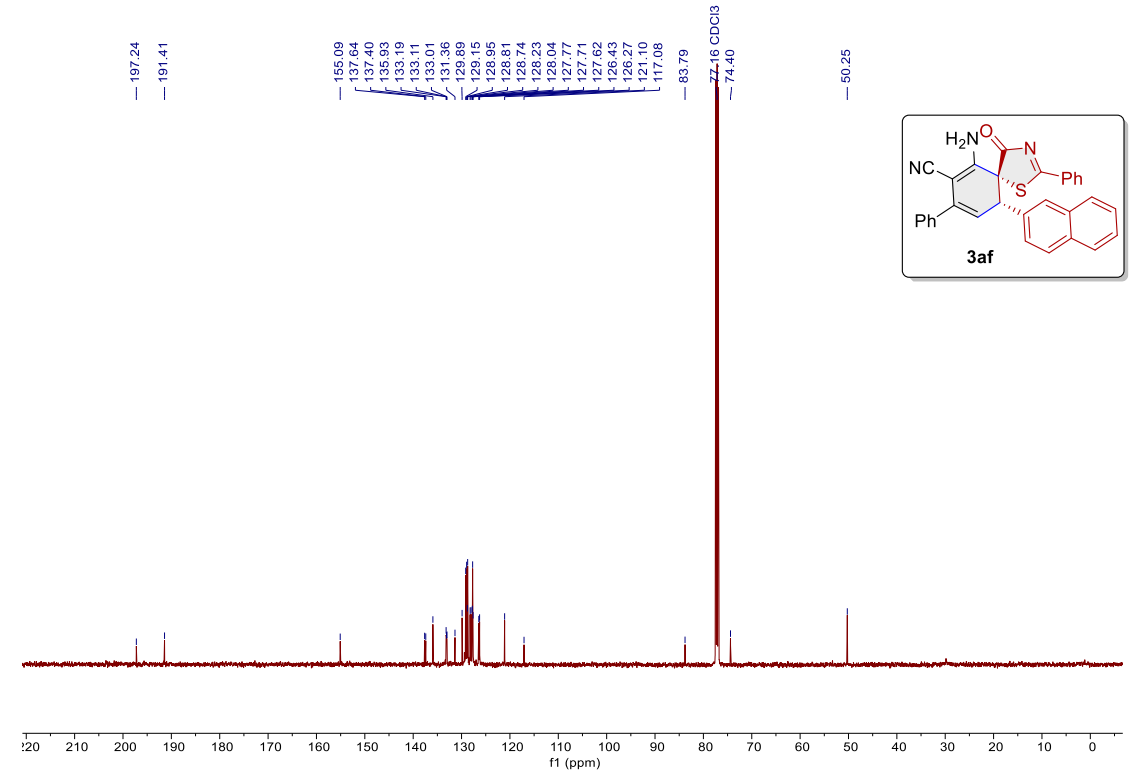
400 MHz ^{1}H NMR spectra of compound **3ae** in $CDCl_3$



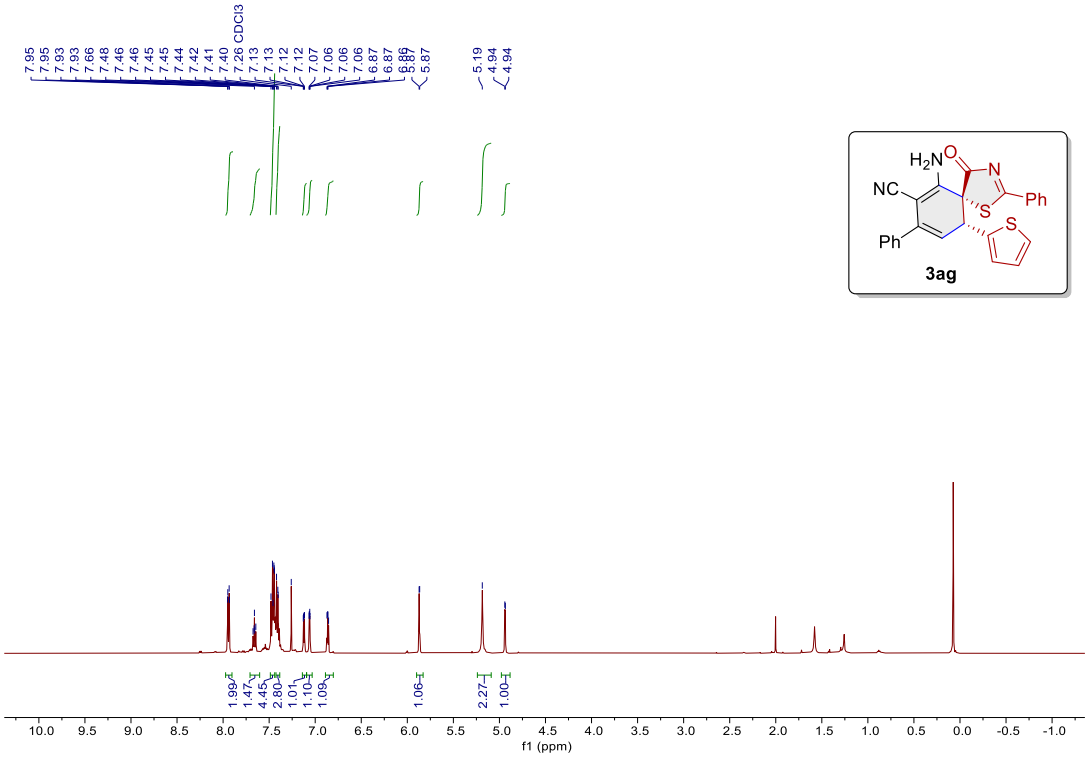
100 MHz $^{13}C\{^{1}H\}$ NMR spectra of compound **3ae** in $CDCl_3$



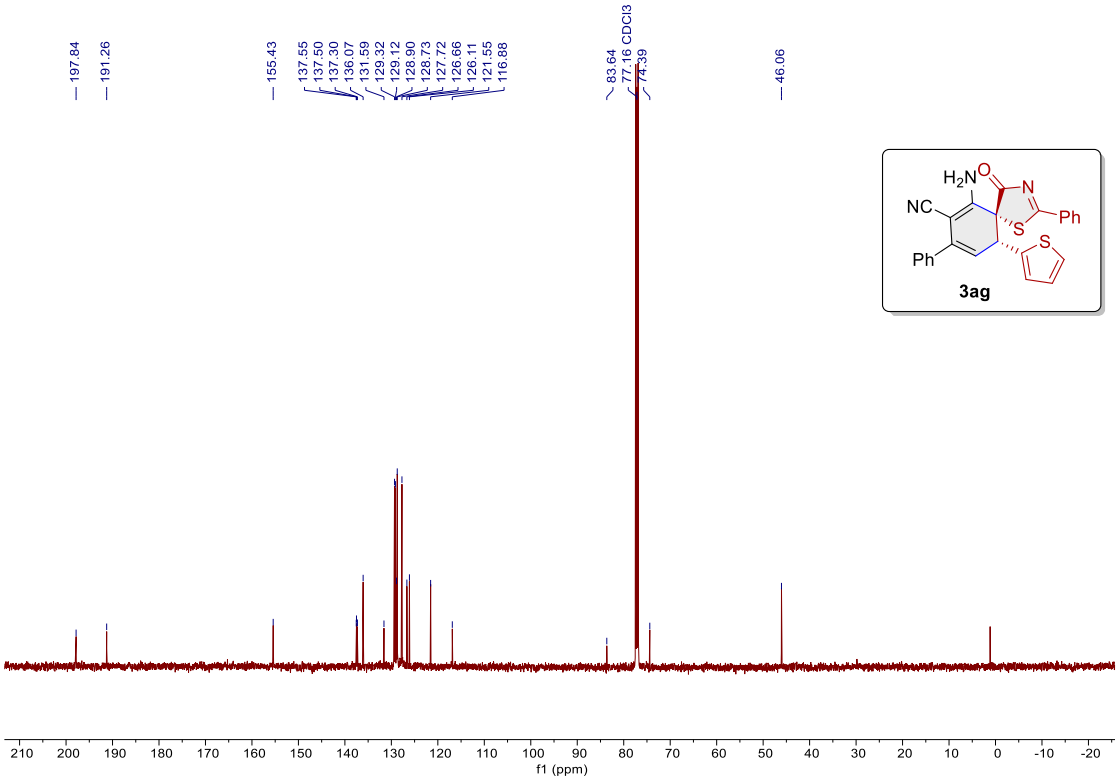
400 MHz ^{1}H NMR spectra of compound **3af** in $CDCl_3$



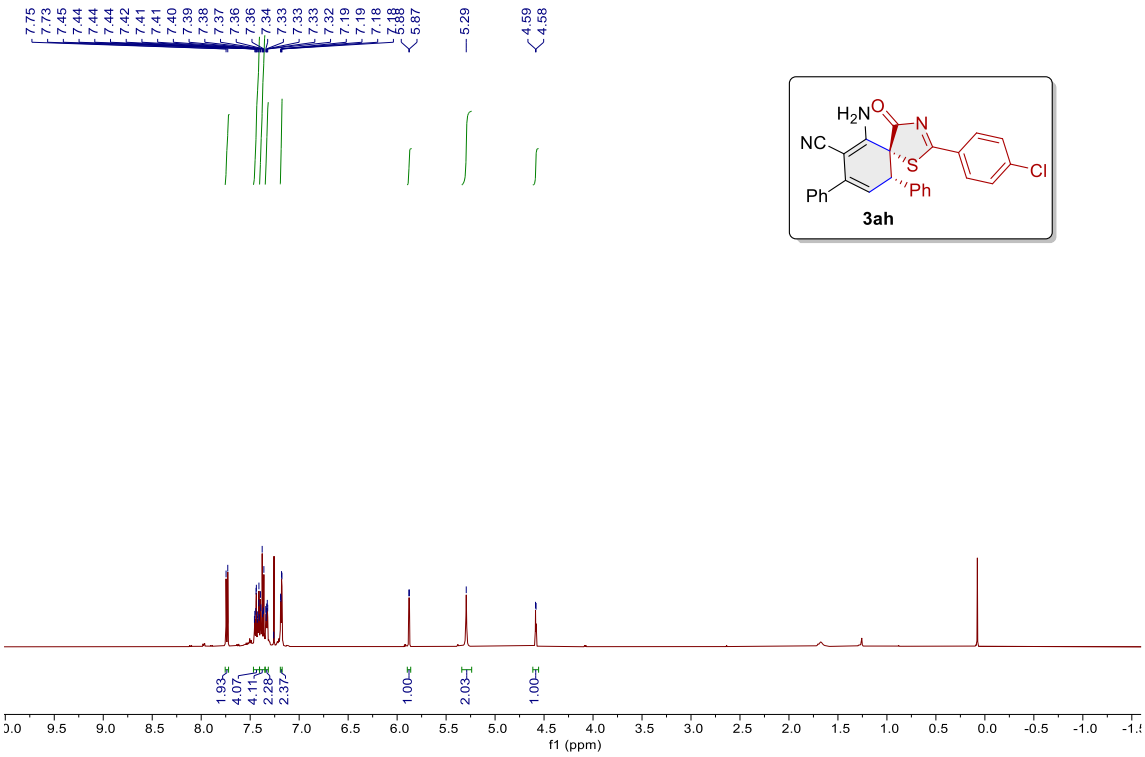
100 MHz $^{13}C\{^{1}H\}$ NMR spectra of compound **3af** in $CDCl_3$



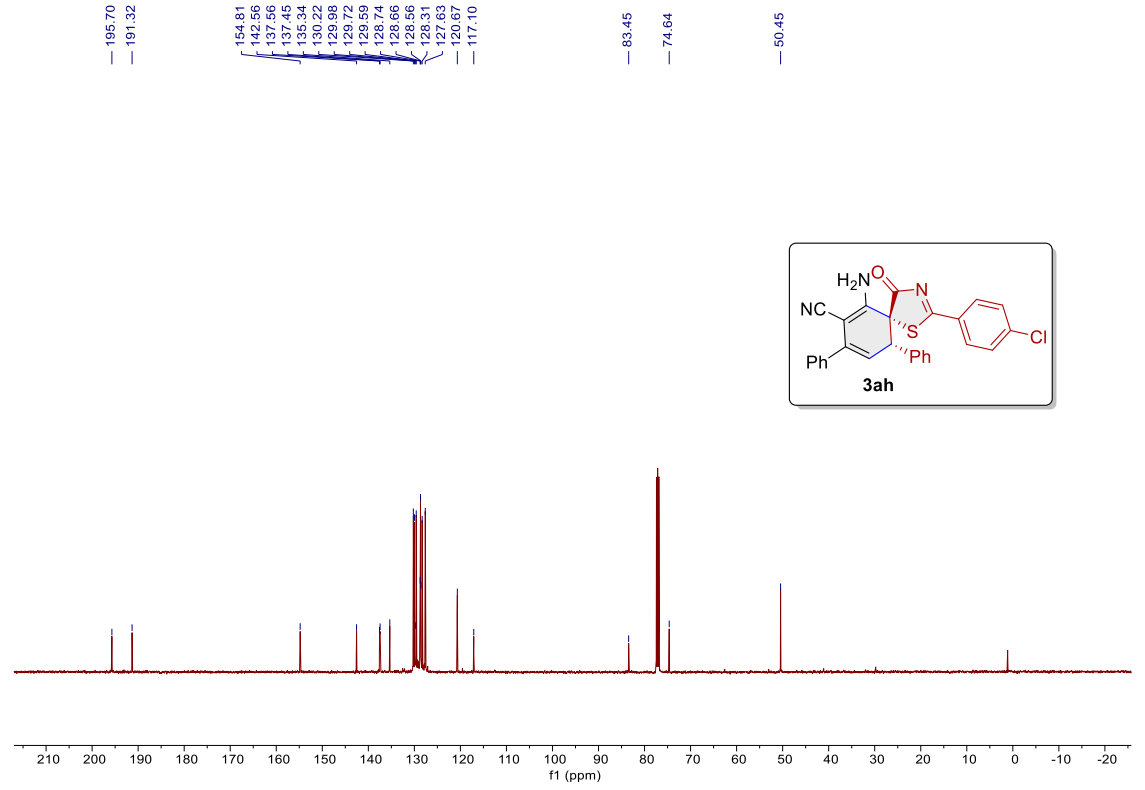
500 MHz ^{1}H NMR spectra of compound **3ag** in $CDCl_3$



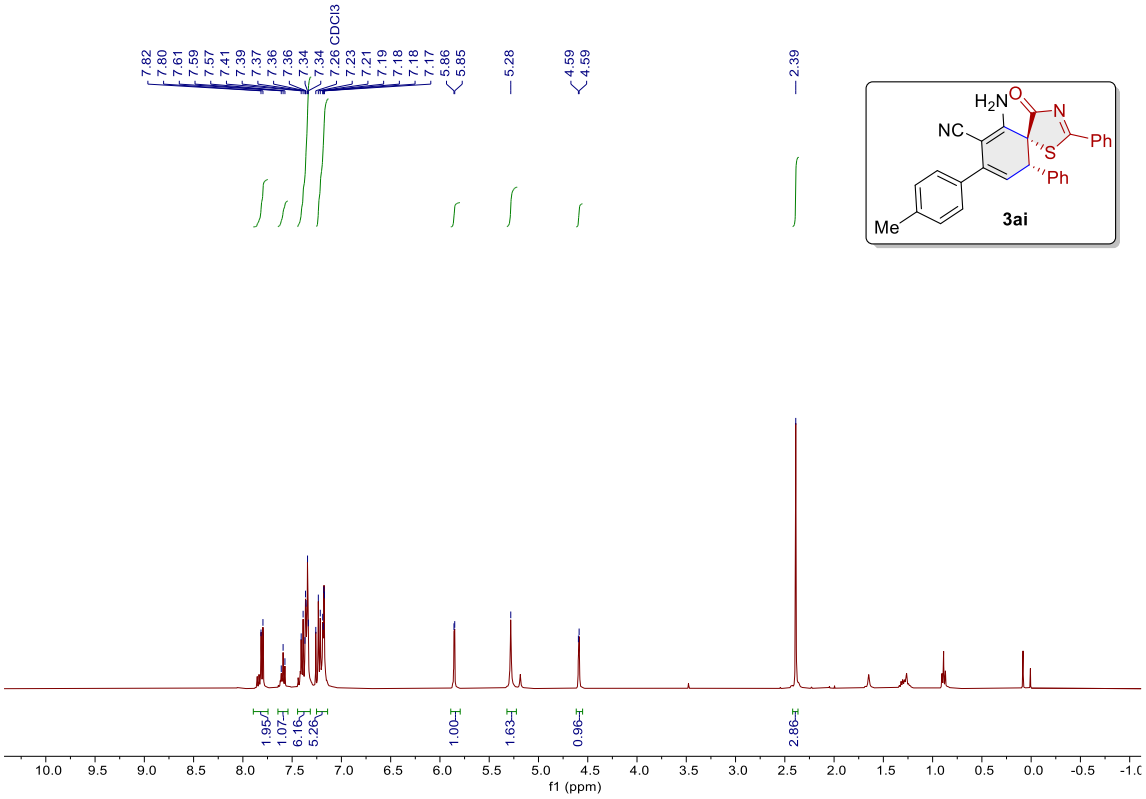
125 MHz ^{13}C{^{1}H} NMR spectra of compound **3ag** in $CDCl_3$



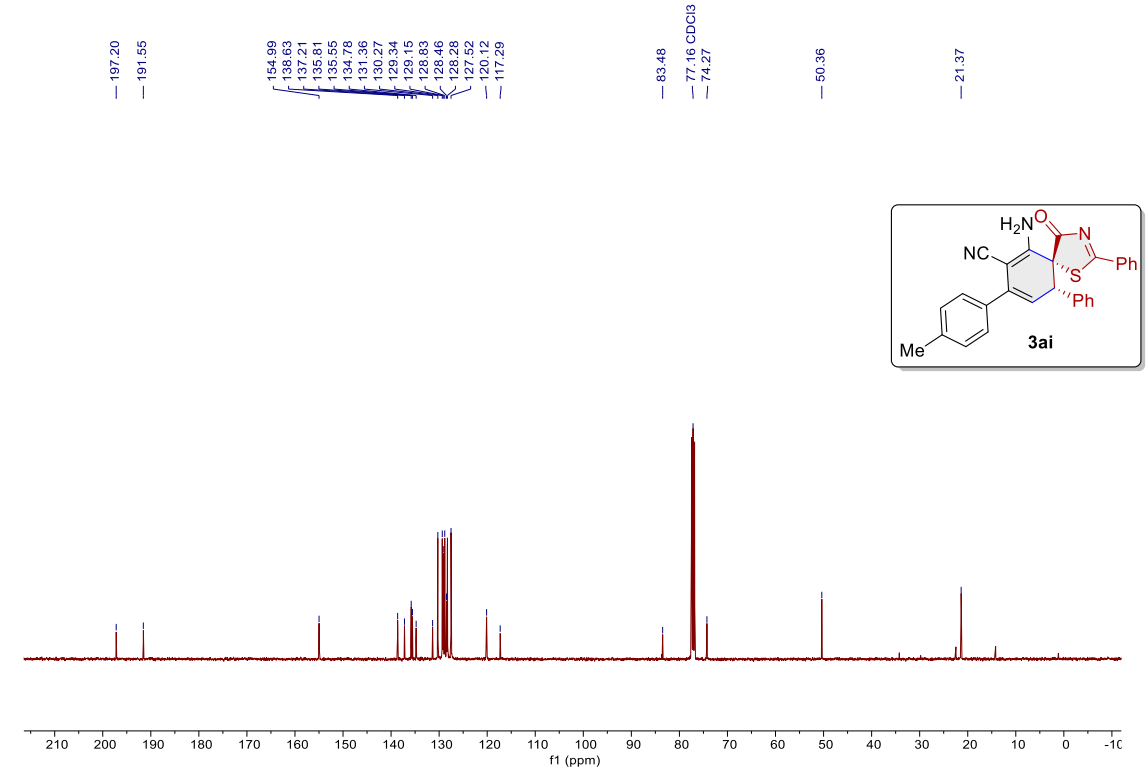
500 MHz ^{1}H NMR spectra of compound **3ah** in $CDCl_3$



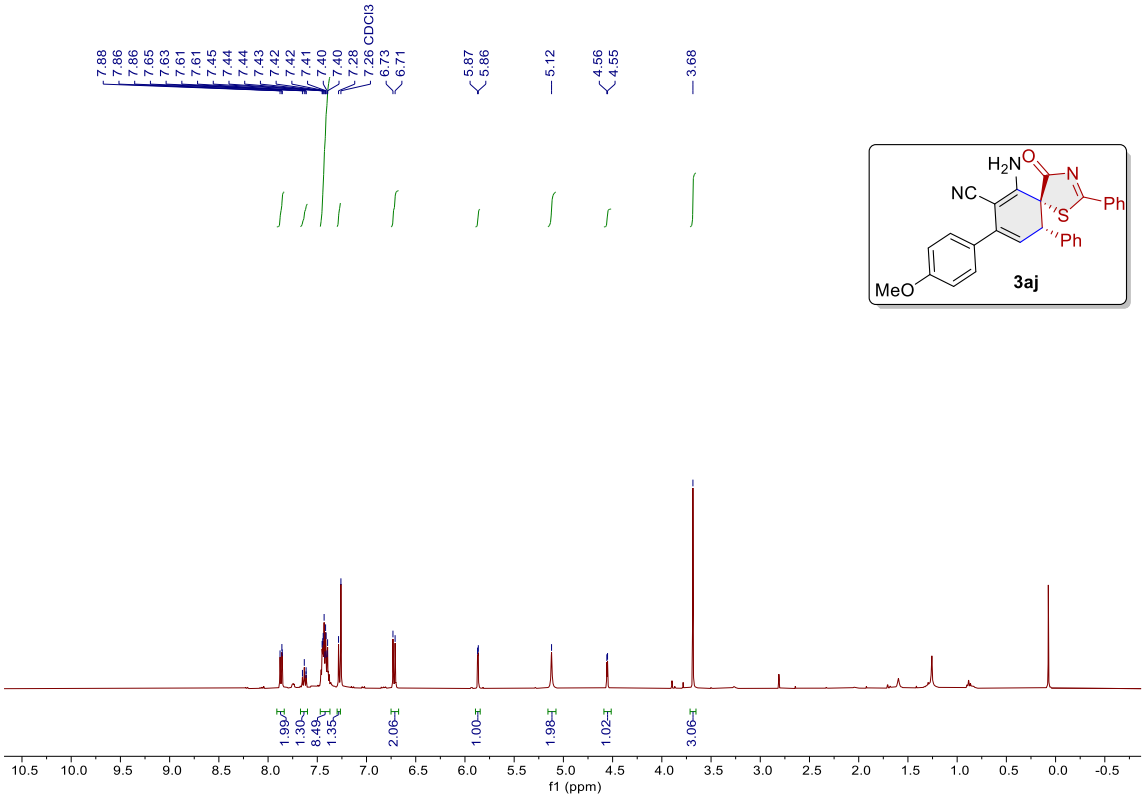
125 MHz $^{13}C\{^{1}H\}$ NMR spectra of compound **3ah** in $CDCl_3$



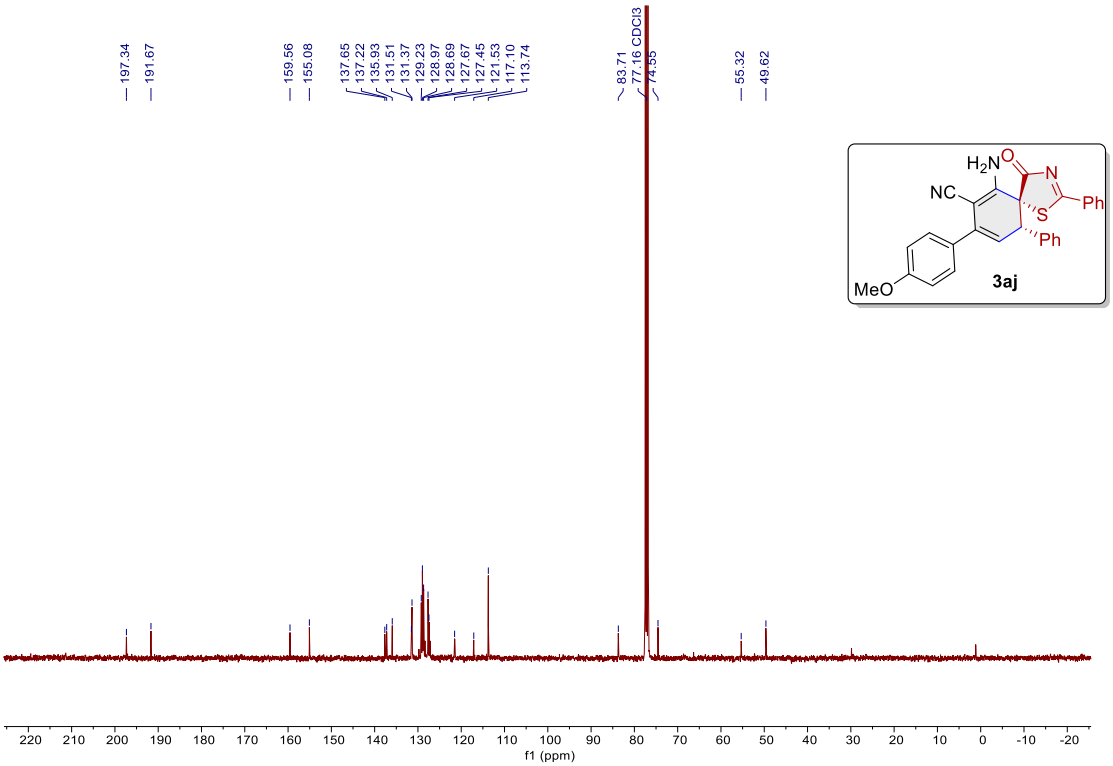
400 MHz ^{1}H NMR spectra of compound **3ai** in $CDCl_3$



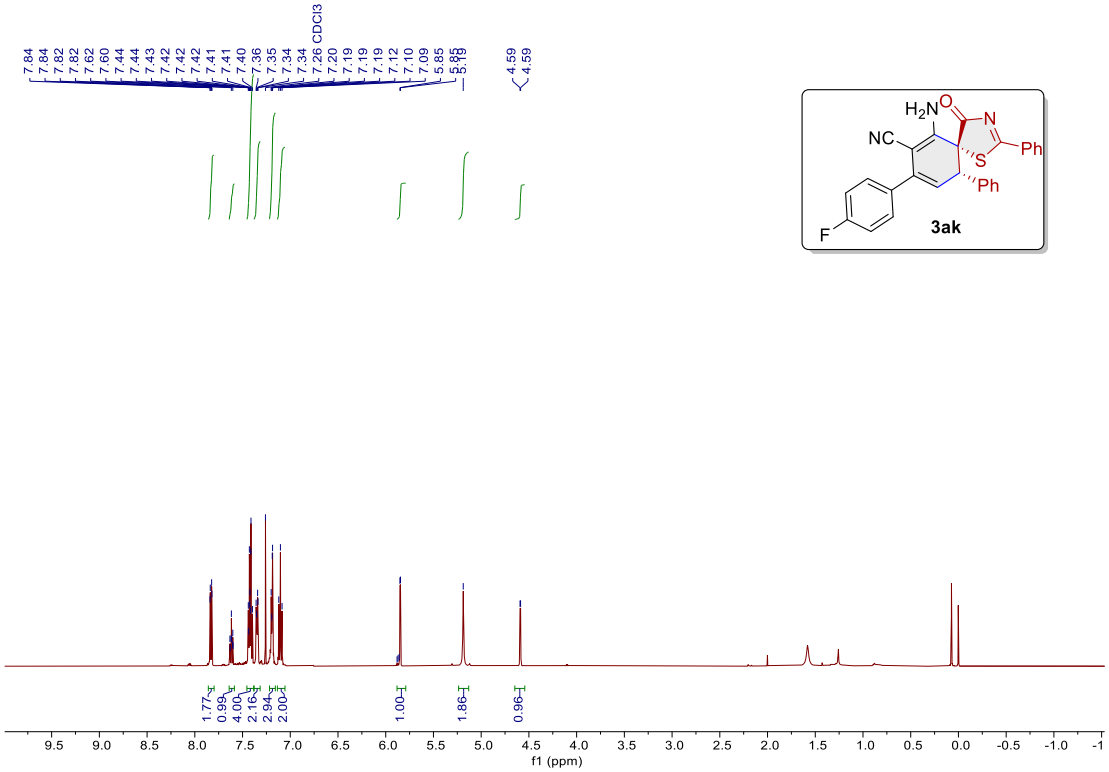
100 MHz $^{13}C\{^{1}H\}$ NMR spectra of compound **3ai** in $CDCl_3$



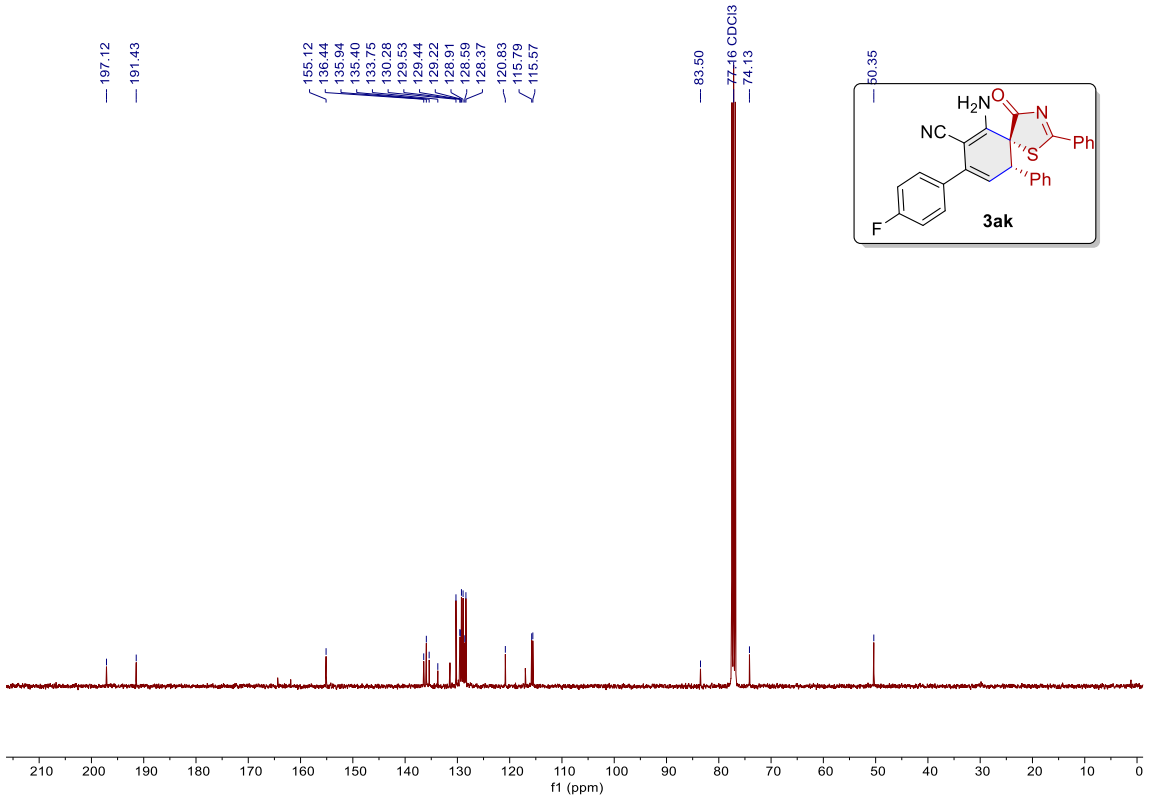
400 MHz ^{1}H NMR spectra of compound **3aj** in $CDCl_3$



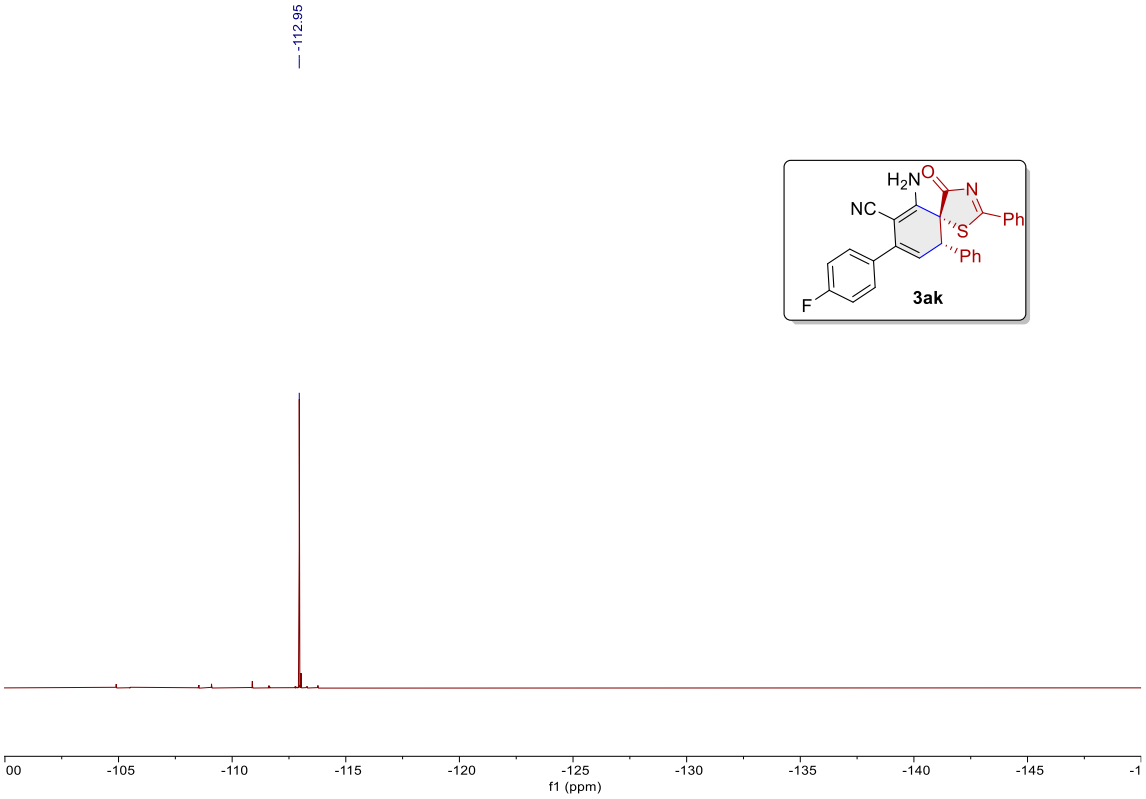
100 MHz $^{13}C\{^{1}H\}$ NMR spectra of compound **3aj** in $CDCl_3$



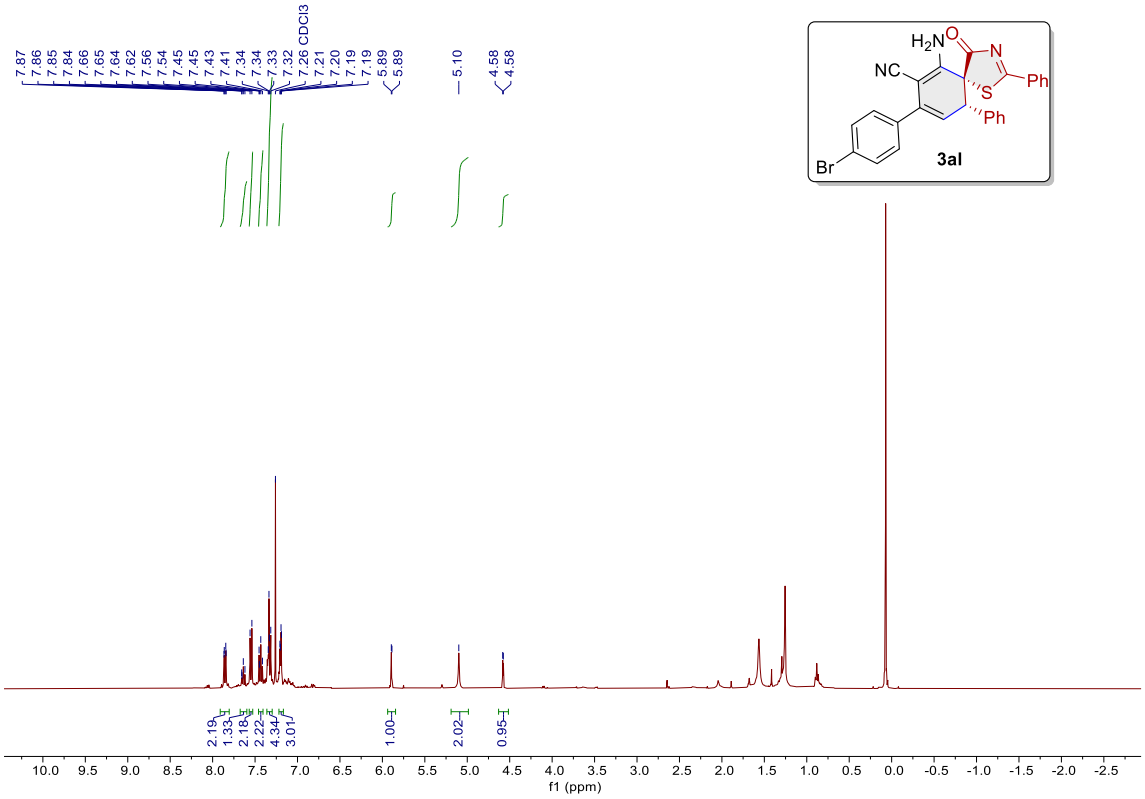
400 MHz ^{1}H NMR spectra of compound **3ak** in $CDCl_3$



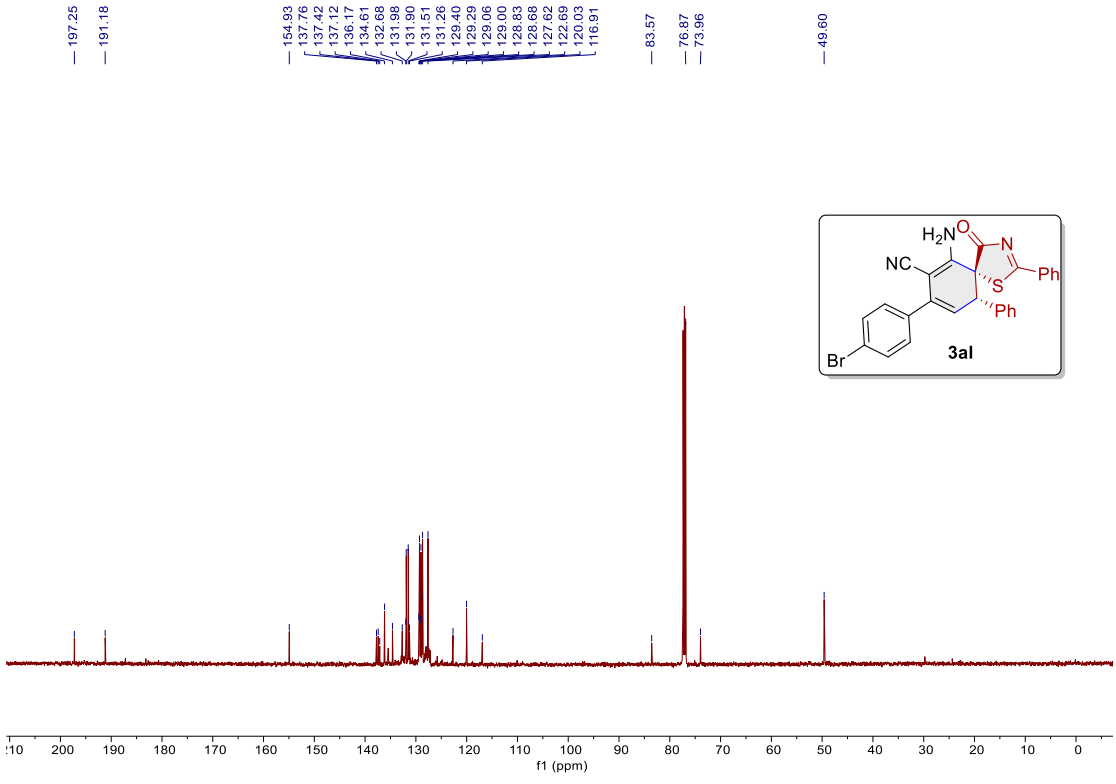
100 MHz $^{13}C\{^{1}H\}$ NMR spectra of compound **3ak**in $CDCl_3$



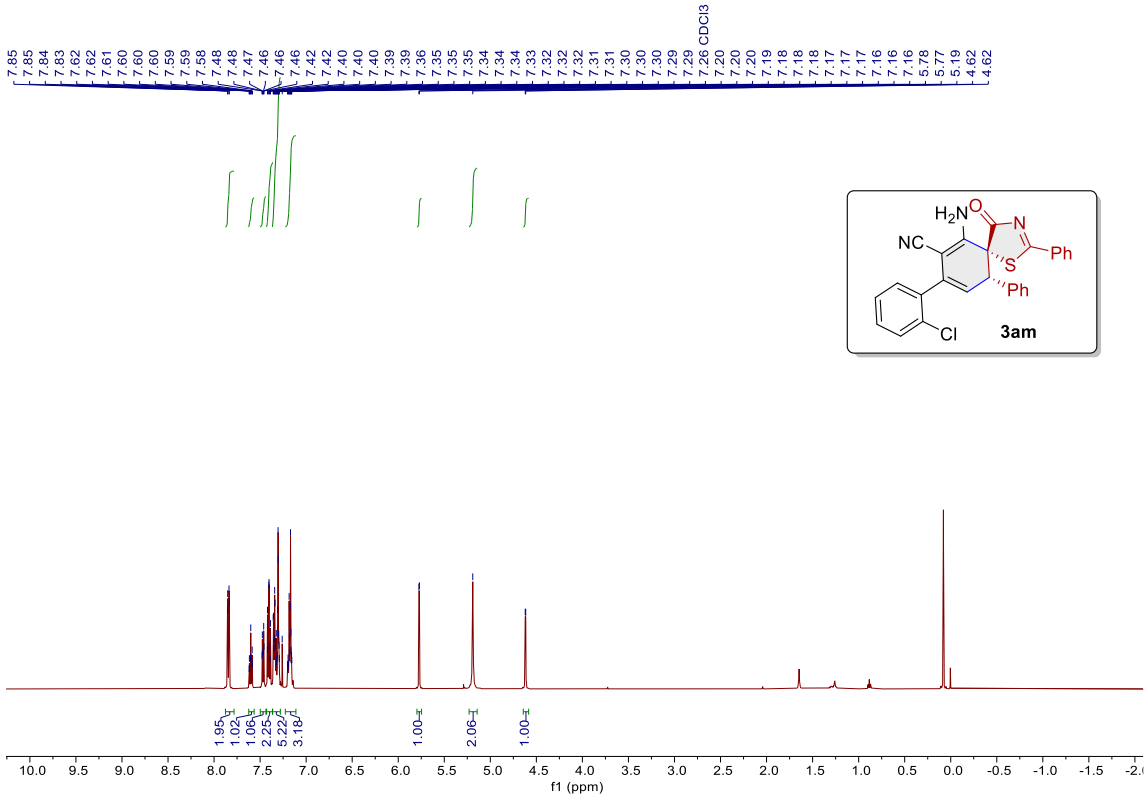
471 MHz $^{19}F\{^{1}H\}$ NMR spectra of compound **3ak** in $CDCl_3$



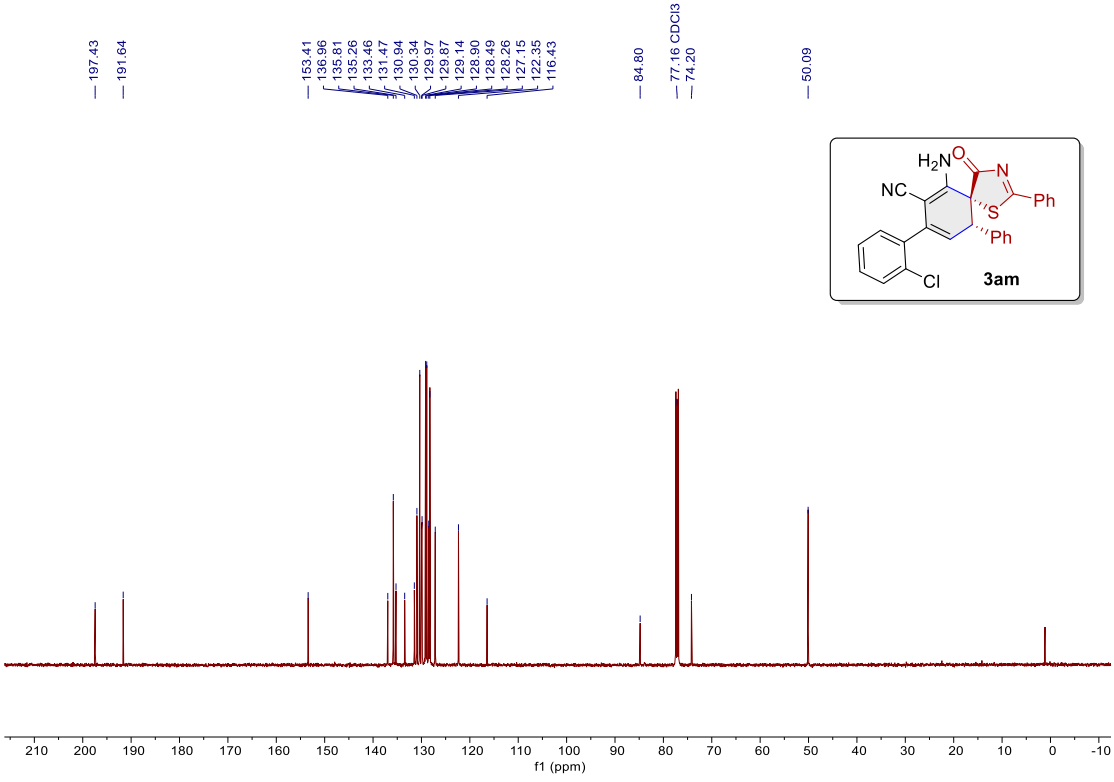
500 MHz ^{1}H NMR spectra of compound **3al** in $CDCl_3$



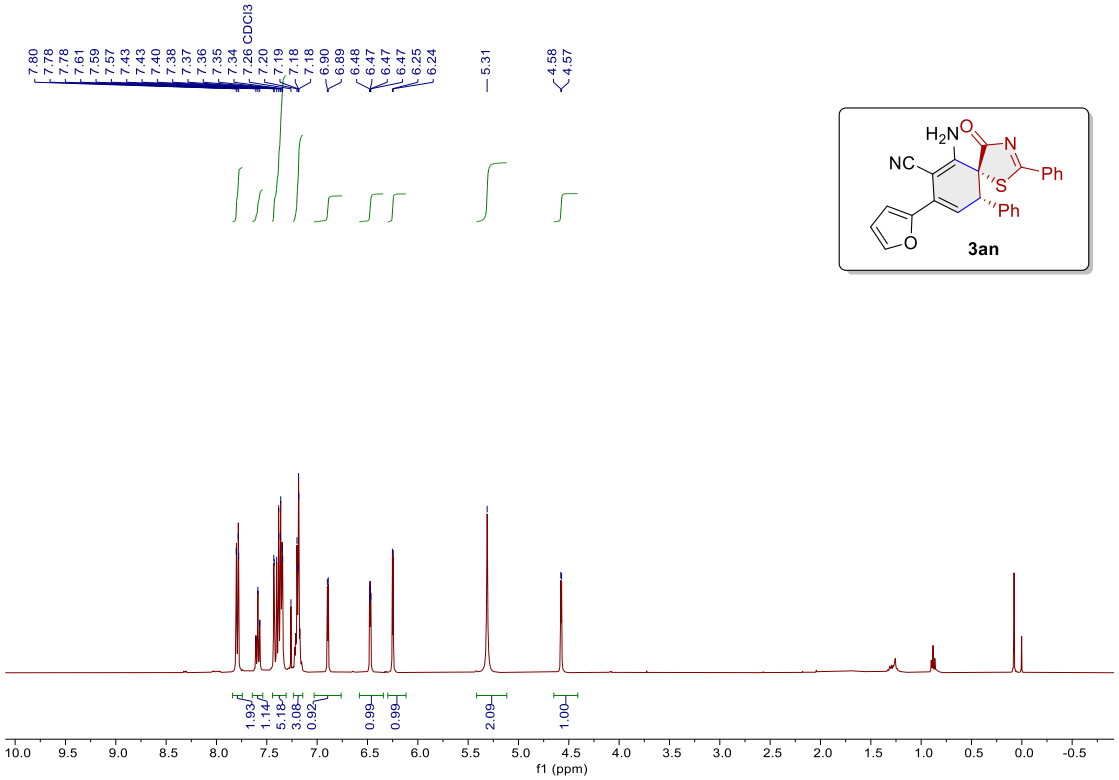
125 MHz ^{13}C{^{1}H} NMR spectra of compound **3al** in $CDCl_3$



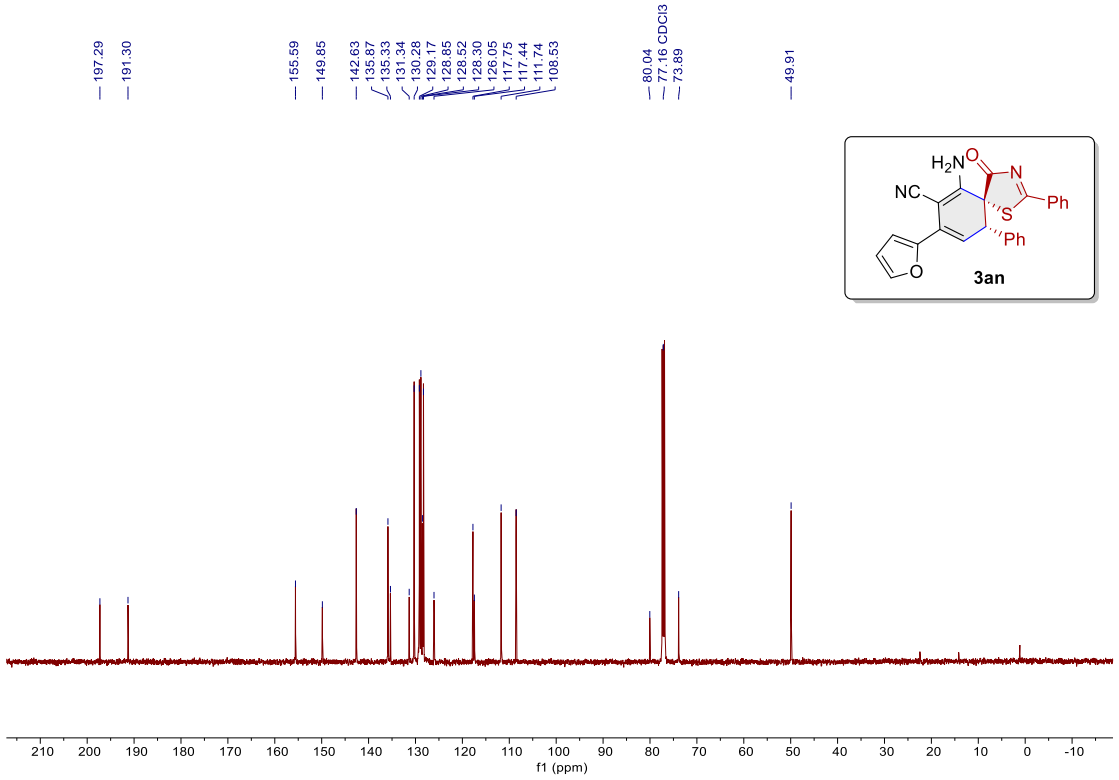
500 MHz ^{1}H NMR spectra of compound **3am** in $CDCl_3$



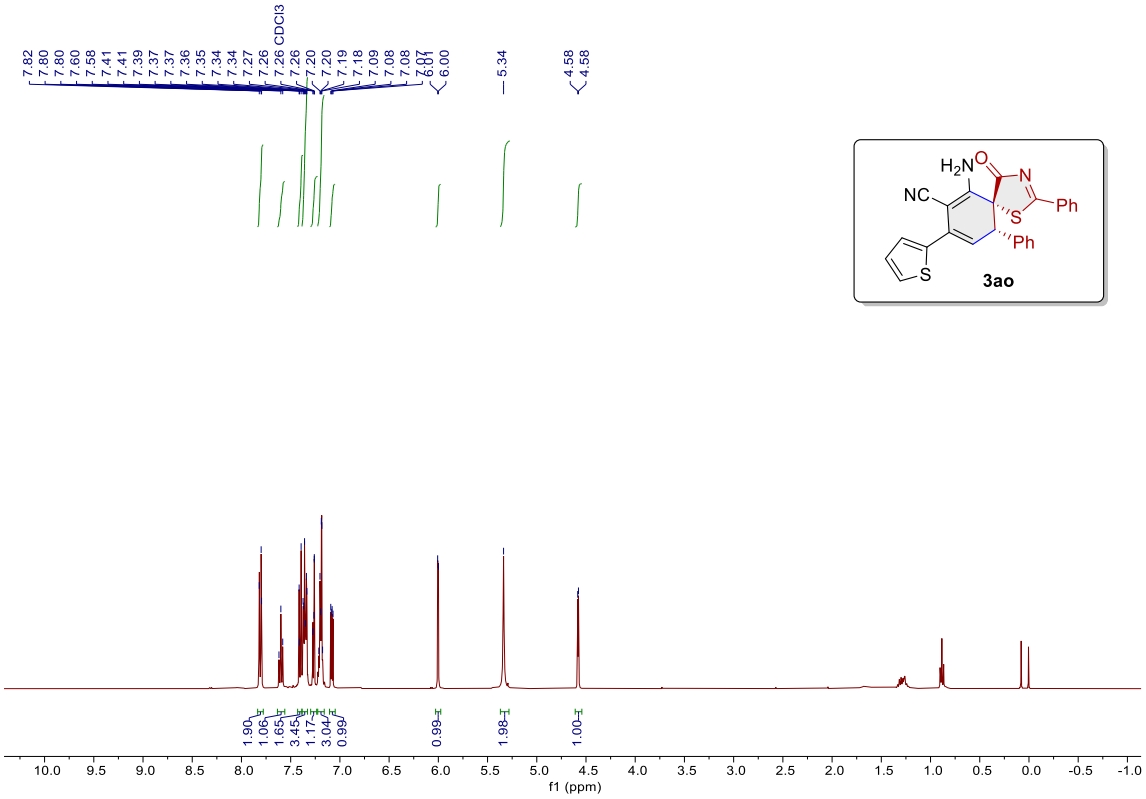
125 MHz ^{13}C{^{1}H} NMR spectra of compound **3am** in $CDCl_3$



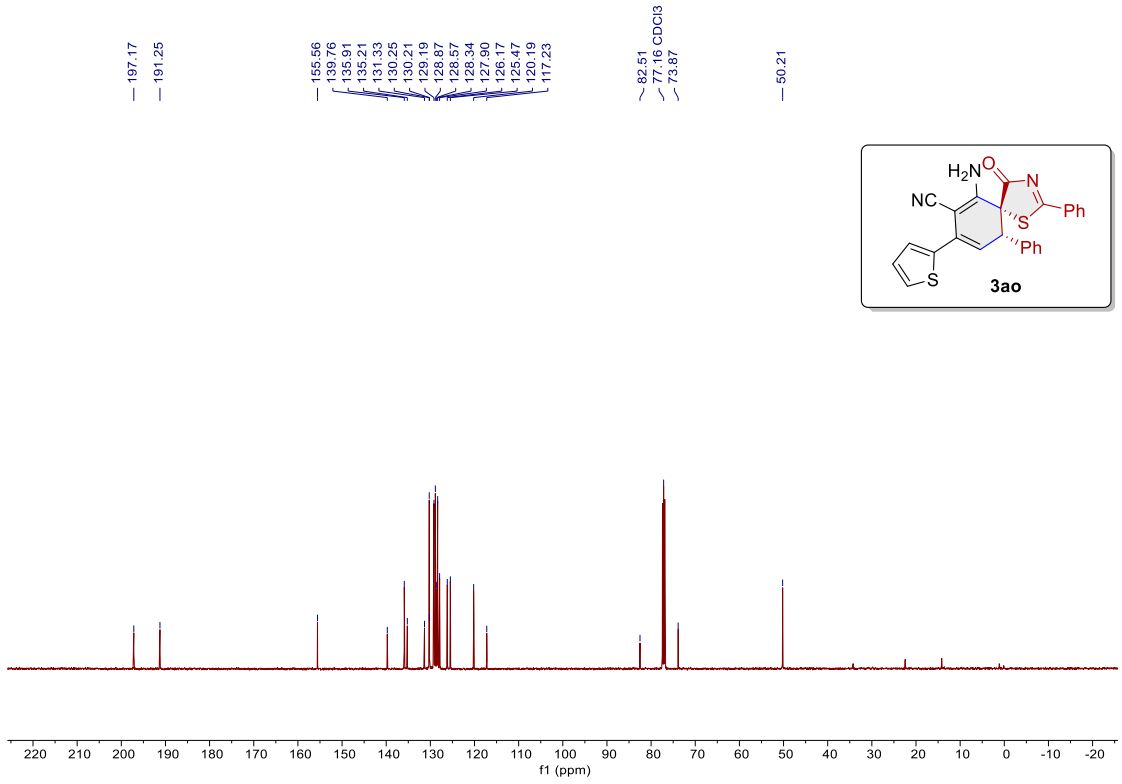
400 MHz ^{1}H NMR spectra of compound **3an** in $CDCl_3$



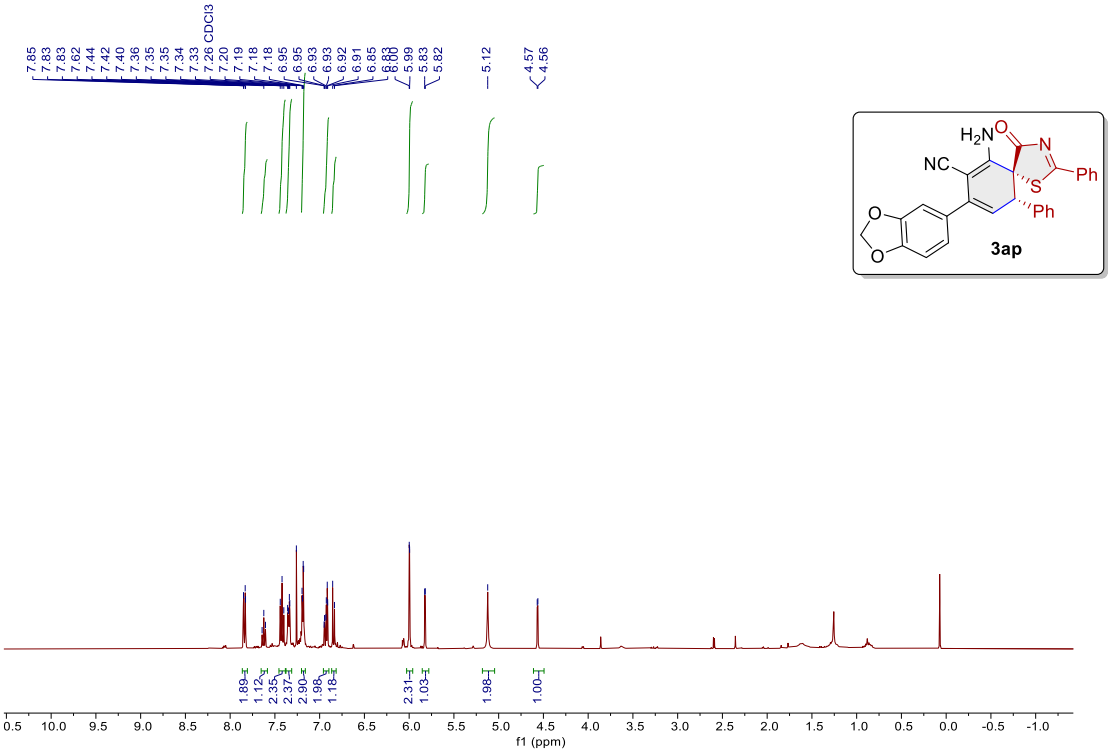
100 MHz ^{13}C{^{1}H} NMR spectra of compound **3an** in $CDCl_3$



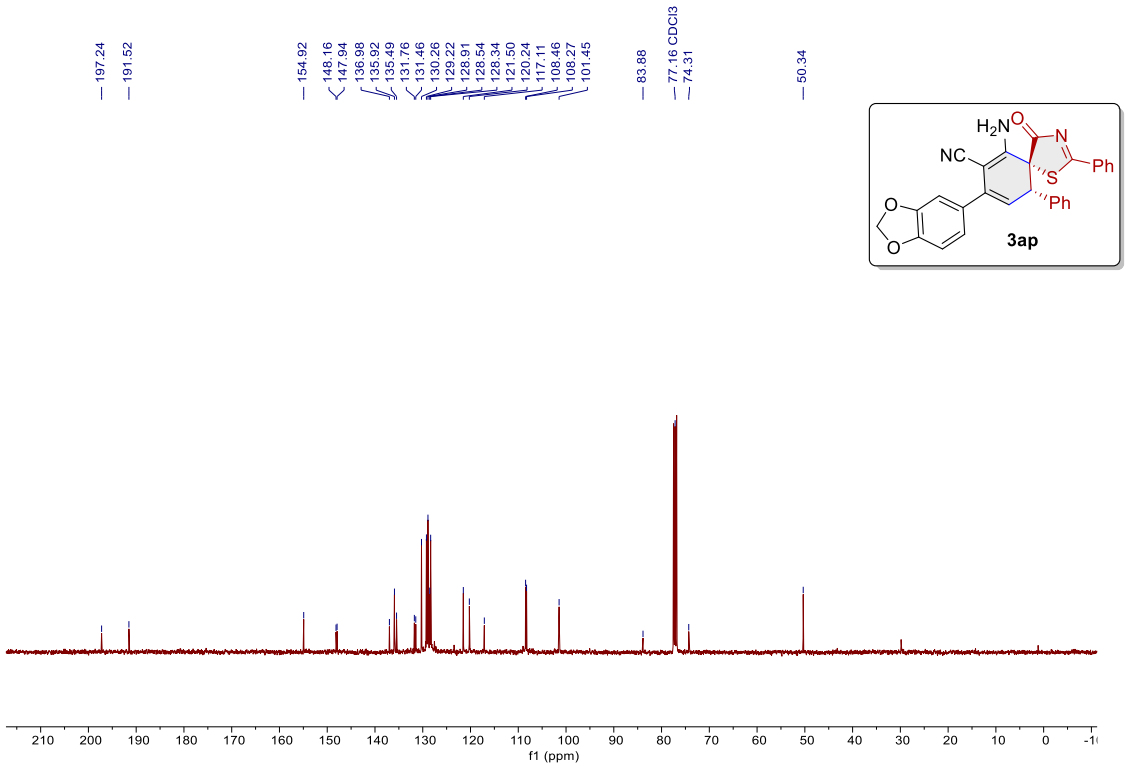
400 MHz ^{1}H NMR spectra of compound **3ao** in $CDCl_3$



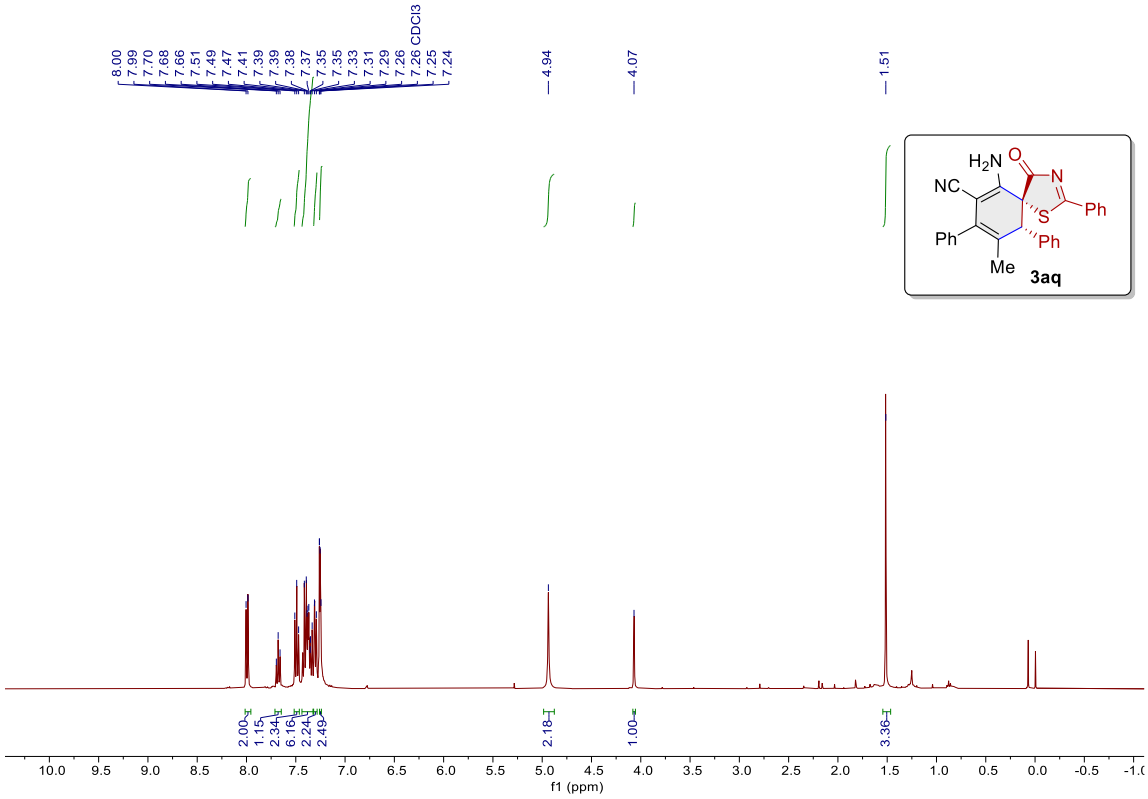
100 MHz ^{13}C{^{1}H} NMR spectra of compound **3ao** in $CDCl_3$



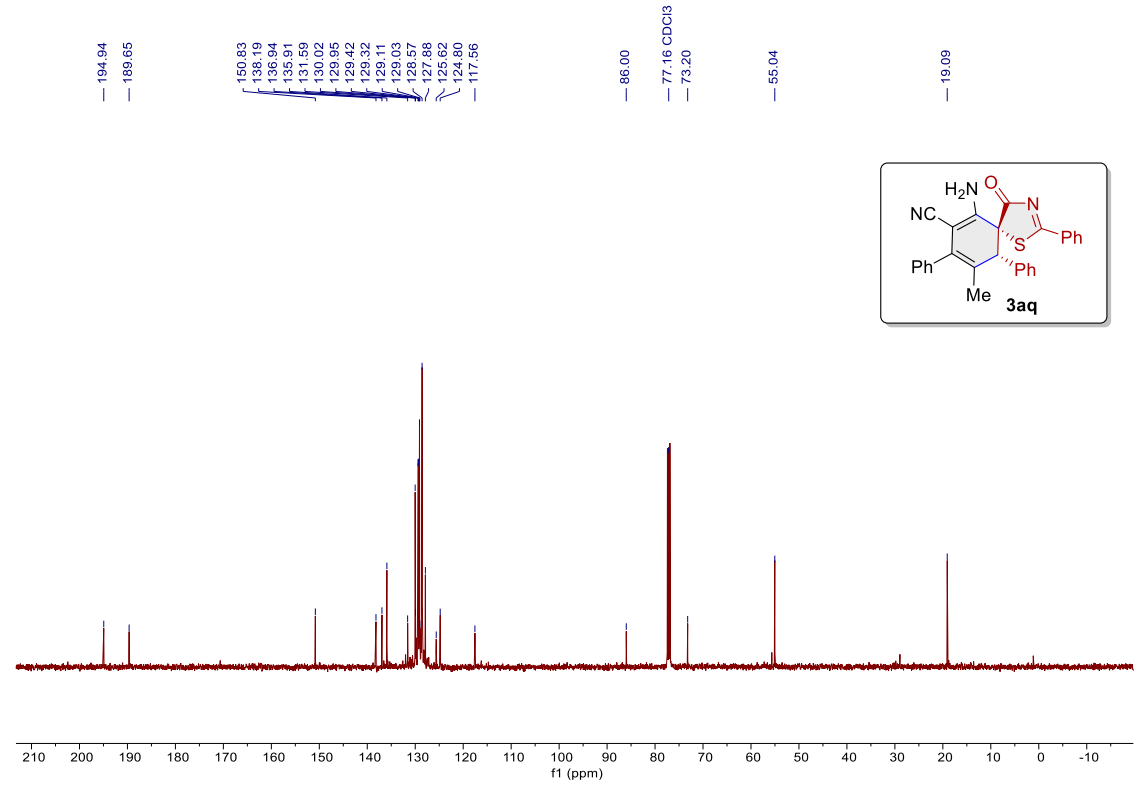
400 MHz ^{1}H NMR spectra of compound **3ap** in $CDCl_3$



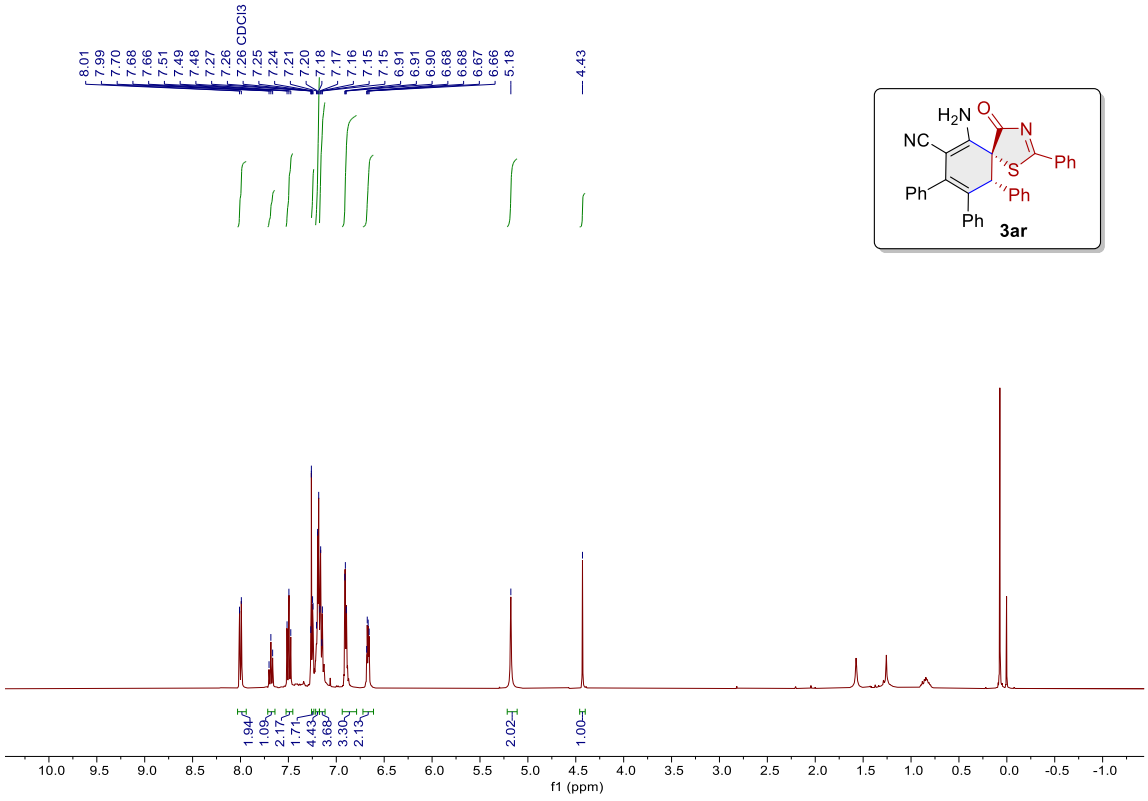
100 MHz ^{13}C{^{1}H} NMR spectra of compound **3ap** in $CDCl_3$



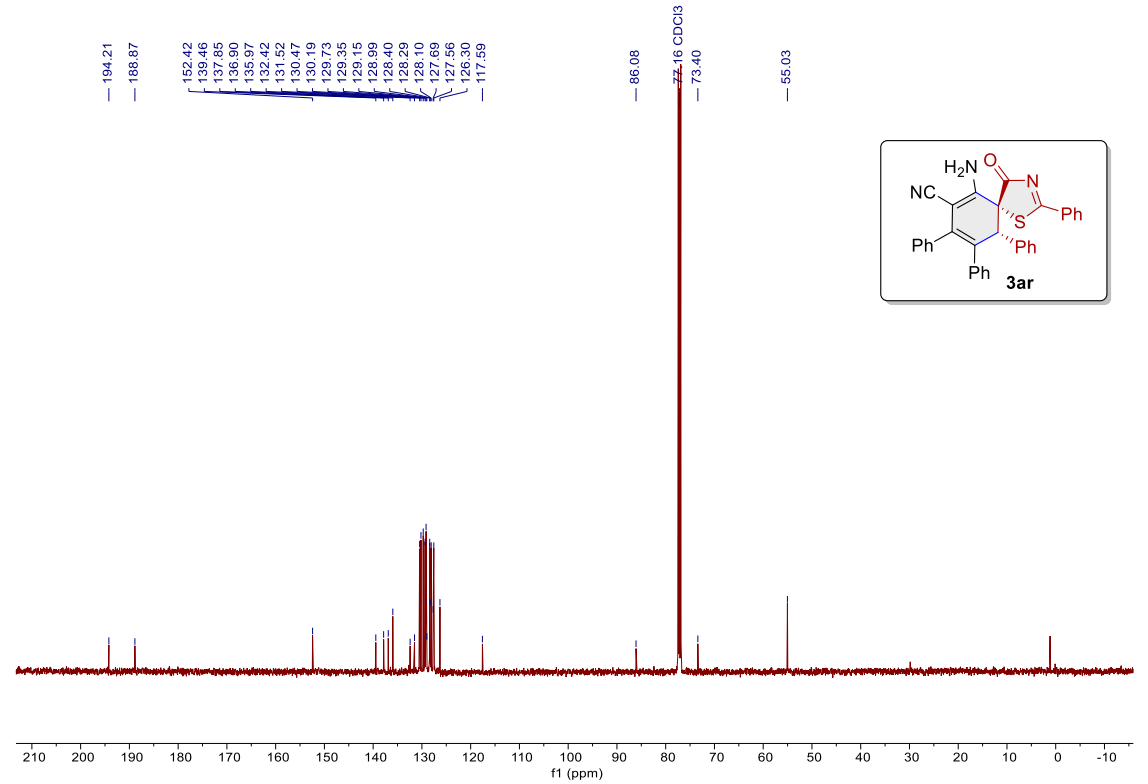
400 MHz ^{1}H NMR spectra of compound **3aq** in $CDCl_3$



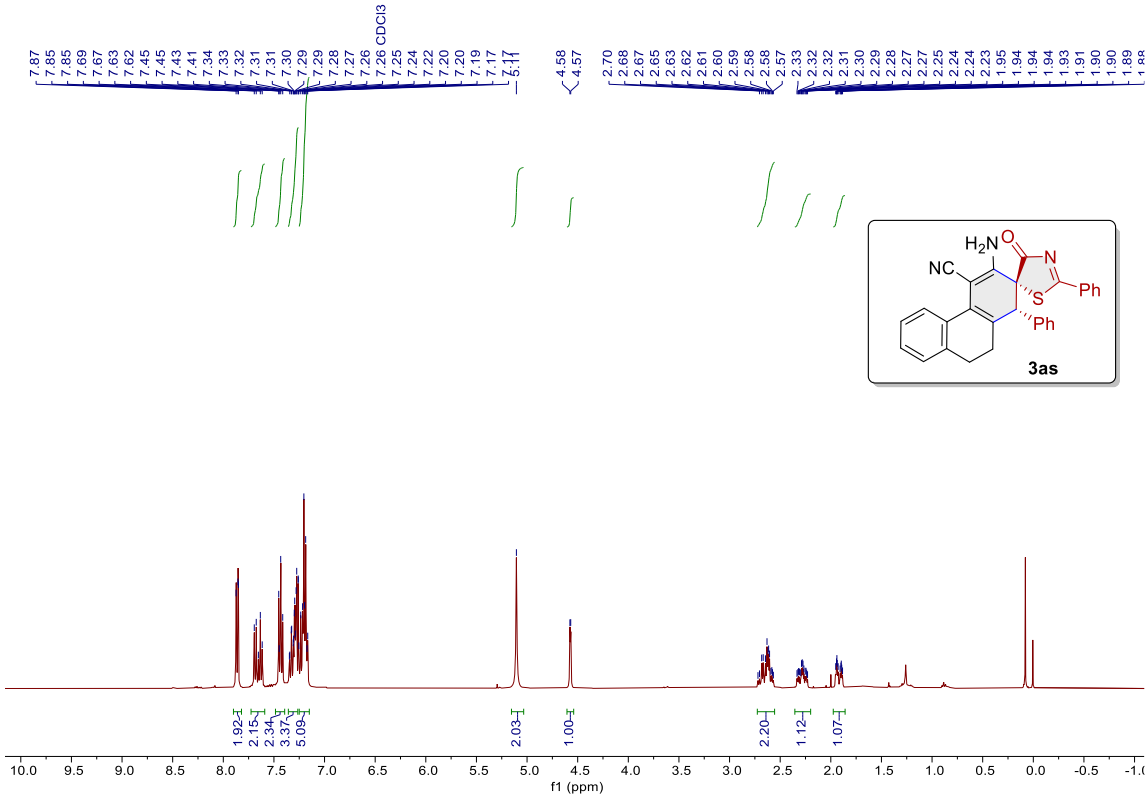
100 MHz ^{13}C{^{1}H} NMR spectra of compound **3aq** in $CDCl_3$



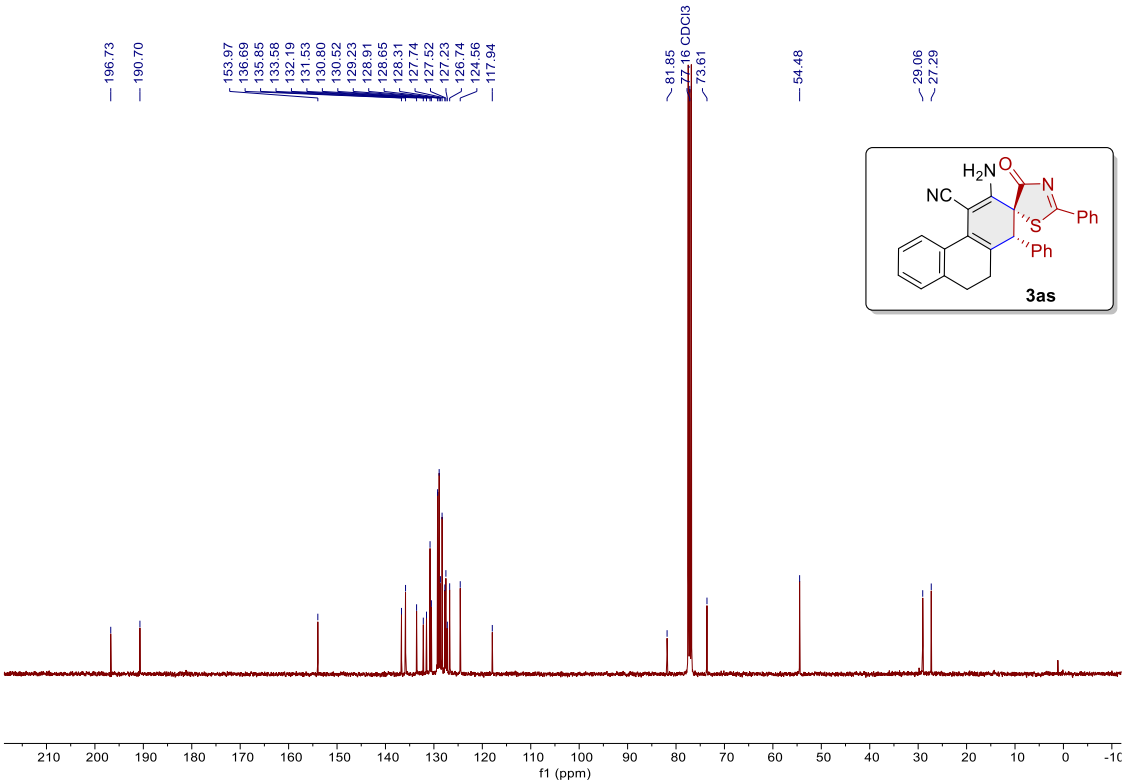
500 MHz ^{1}H NMR spectra of compound **3ar** in $CDCl_3$



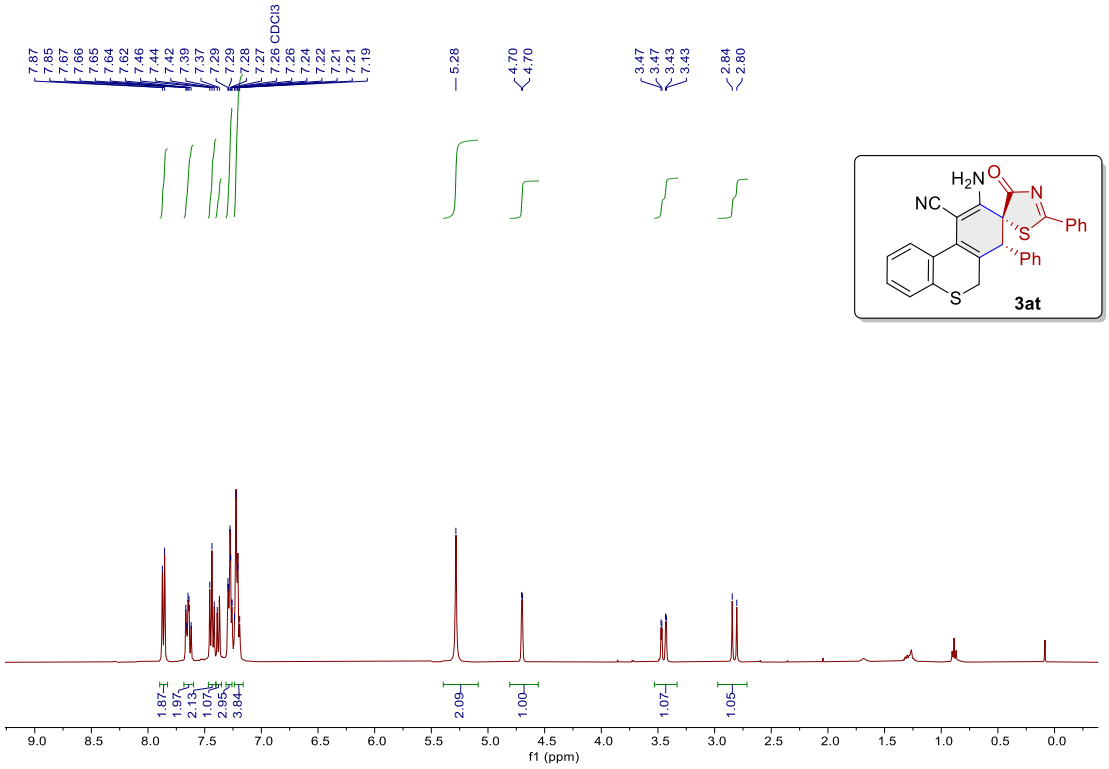
125 MHz ^{13}C{^{1}H} NMR spectra of compound **3ar** in $CDCl_3$



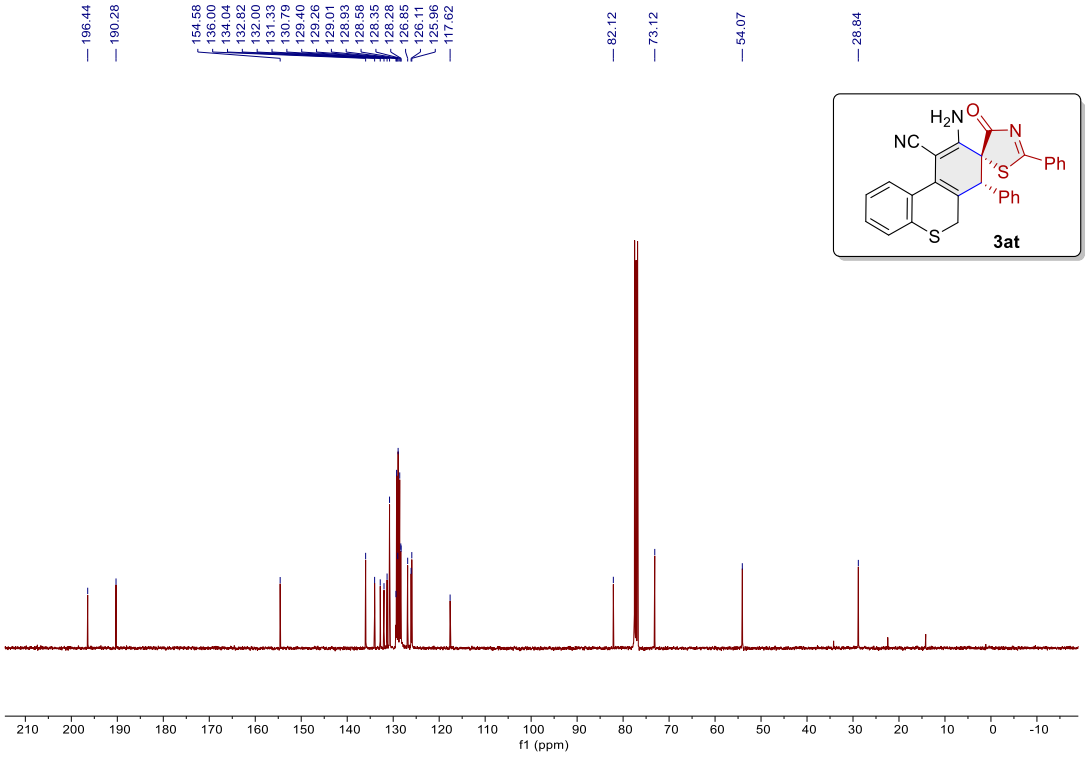
400 MHz ^{1}H NMR spectra of compound **3as** in $CDCl_3$



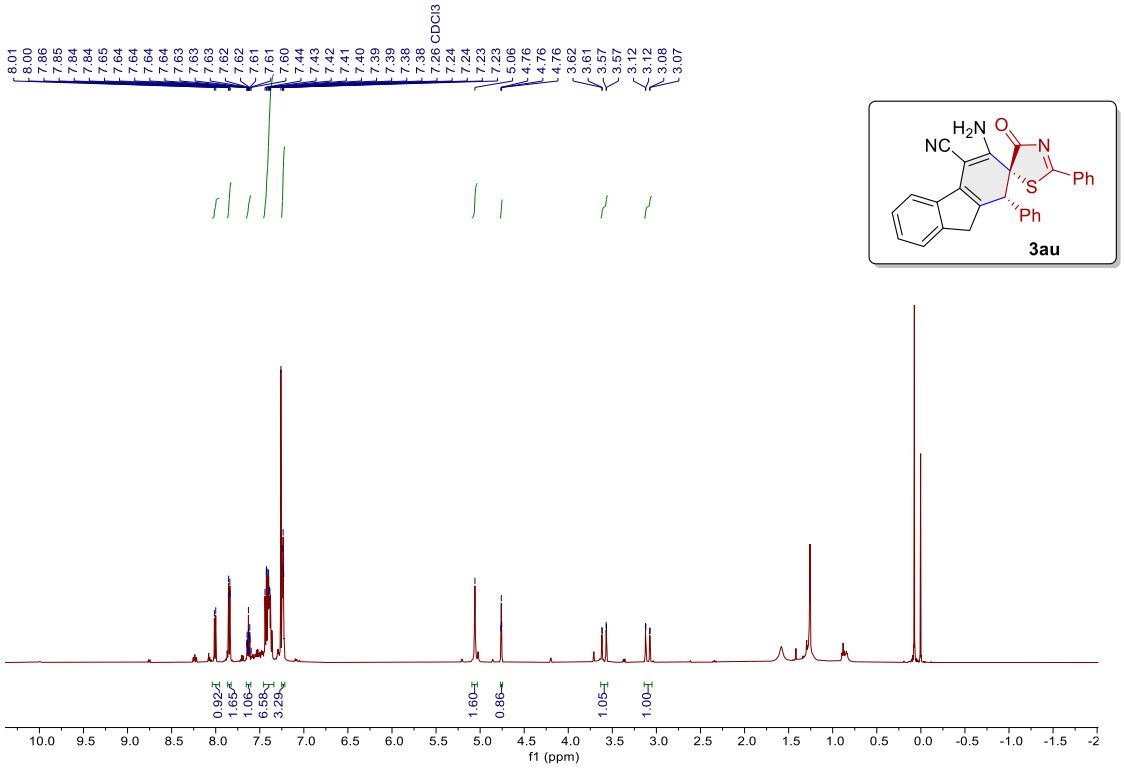
100 MHz $^{13}C\{^{1}H\}$ NMR spectra of compound **3as** in $CDCl_3$



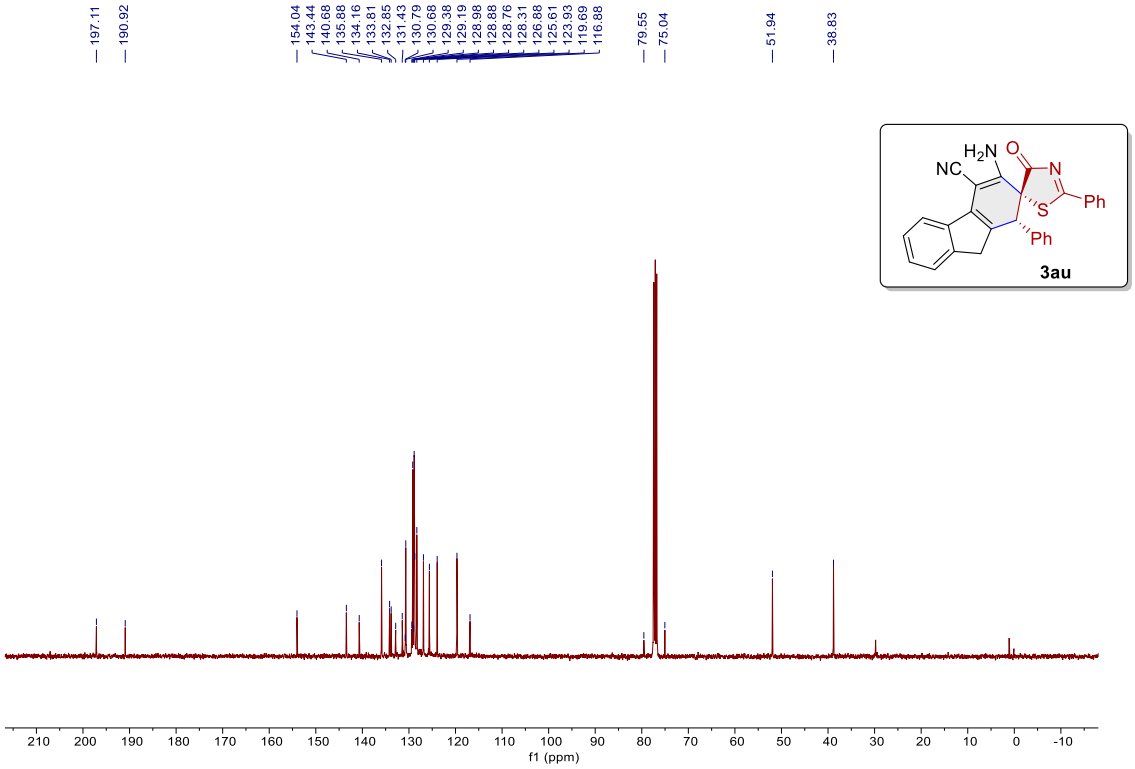
400 MHz ^{1}H NMR spectra of compound **3at** in $CDCl_3$



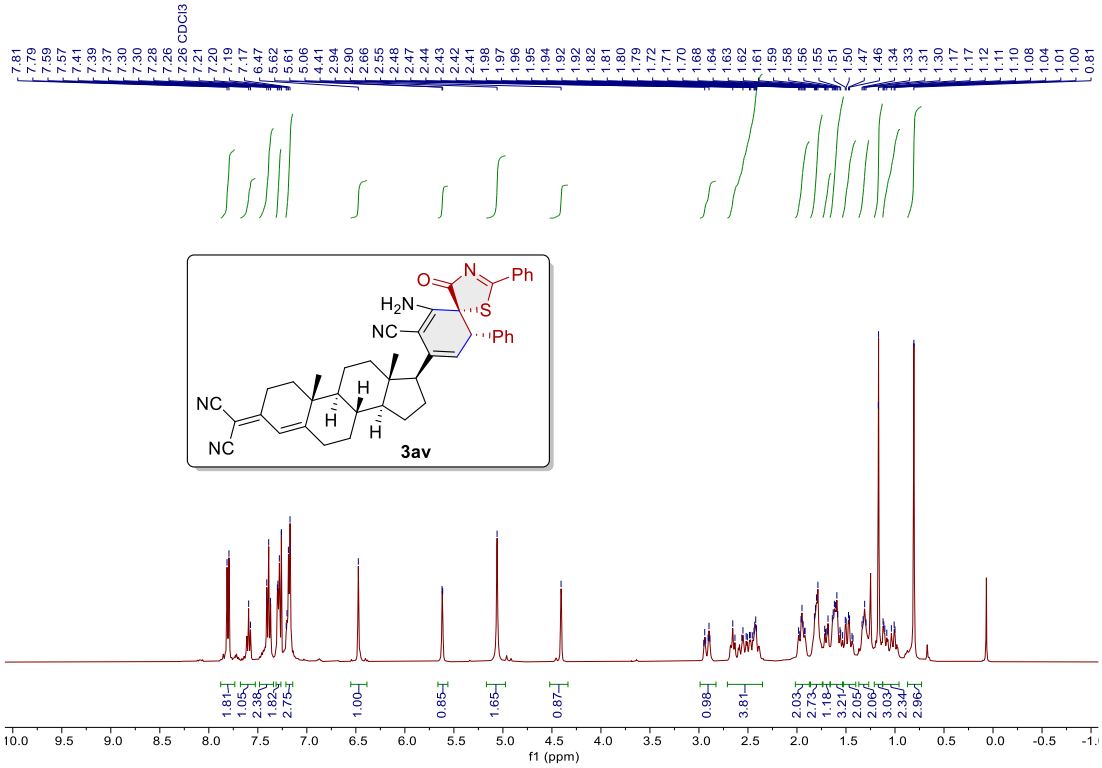
100 MHz ^{13}C{^{1}H} NMR spectra of compound **3at** in $CDCl_3$



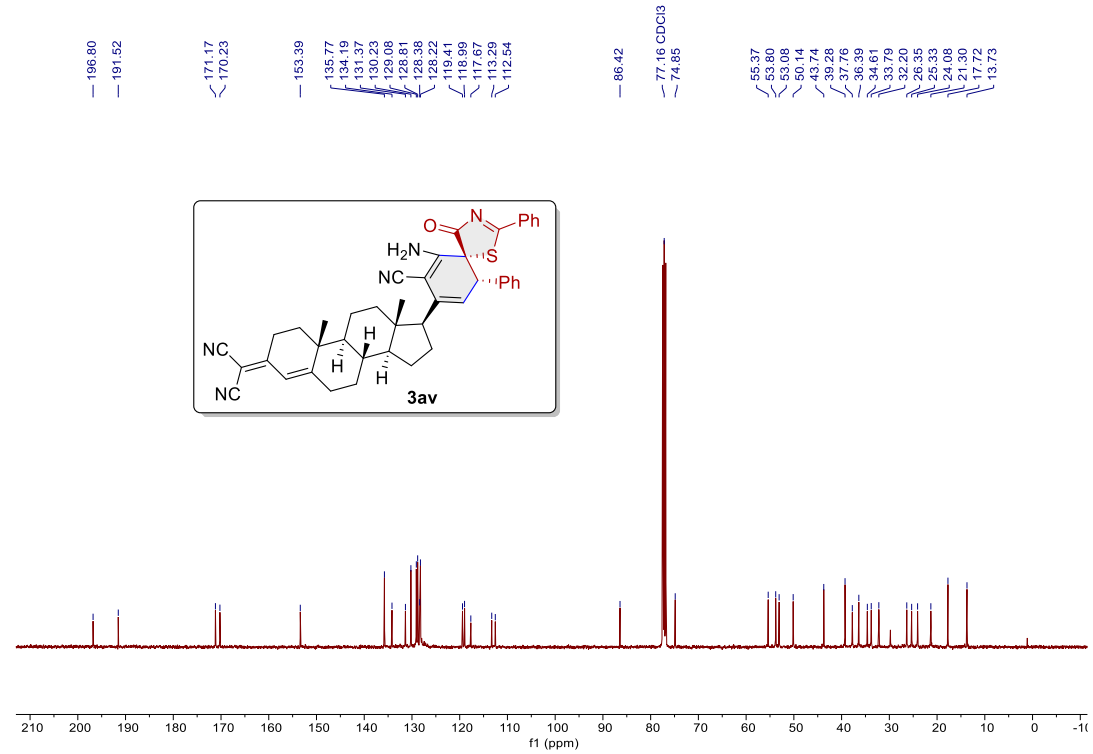
500 MHz ^{1}H NMR spectra of compound **3au** in $CDCl_3$



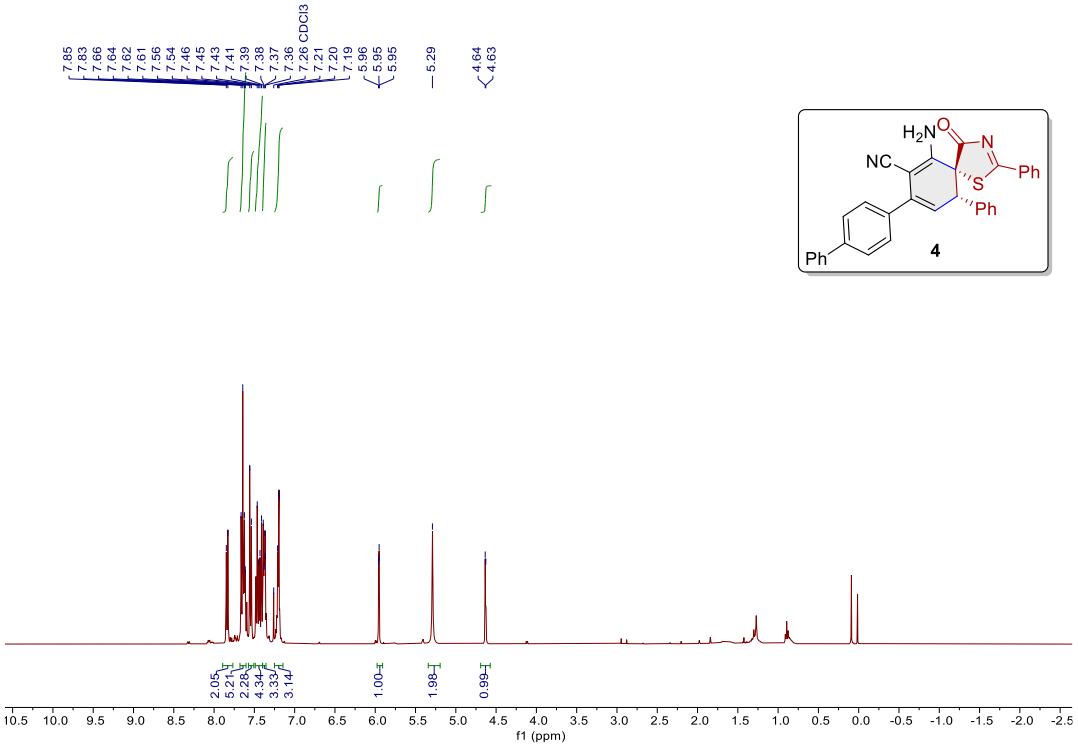
125 MHz ^{13}C{^{1}H} NMR spectra of compound **3au** in $CDCl_3$



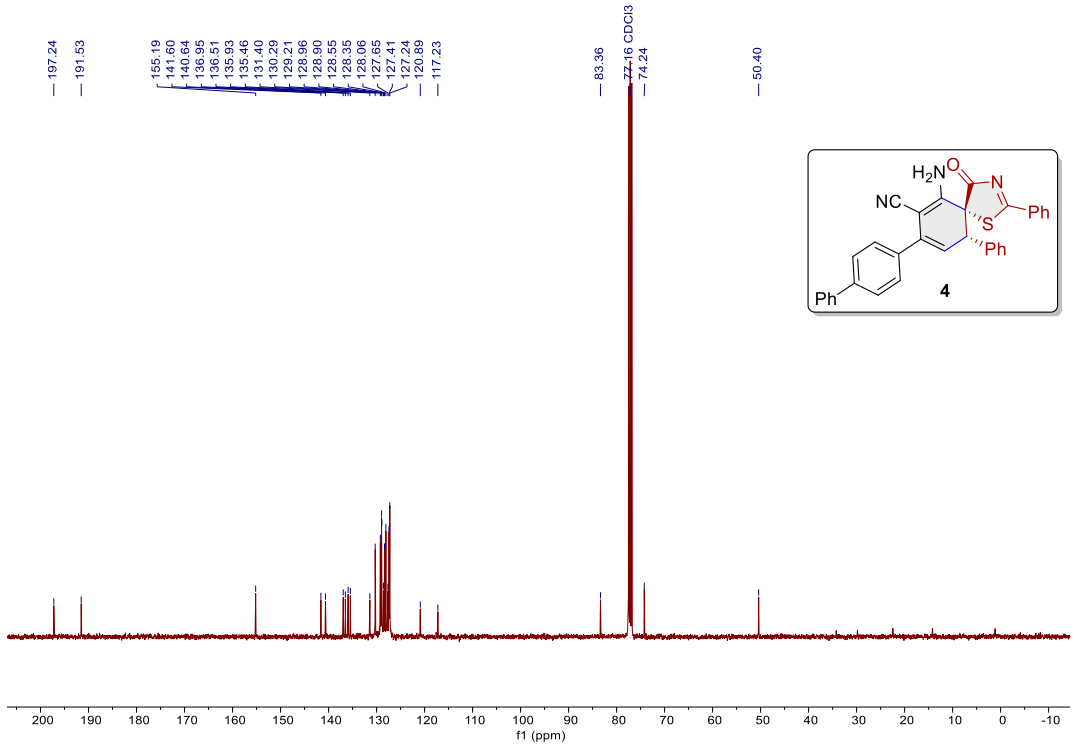
400 MHz ^{1}H NMR spectra of compound **3av** in $CDCl_3$



100 MHz $^{13}C\{^{1}H\}$ NMR spectra of compound **3av** in $CDCl_3$

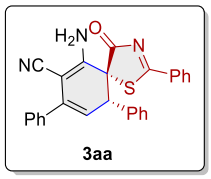


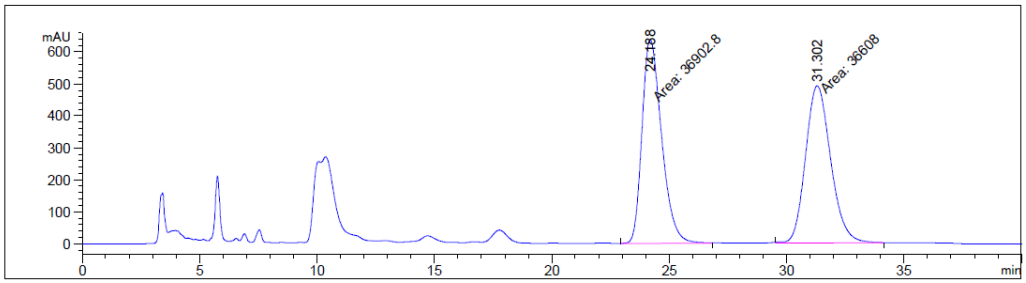
400 MHz ^{1}H NMR spectra of compound **4** in $CDCl_3$



100 MHz ^{13}C{^{1}H} NMR spectra of compound **4** in $CDCl_3$

HPLC spectra:

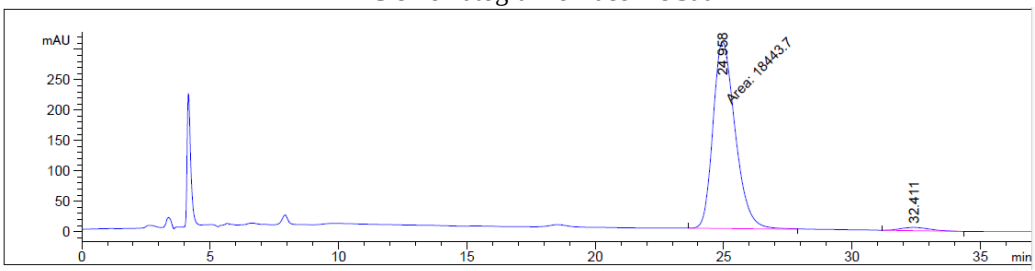




Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.188	MF	0.9657	3.69028e4	636.90961	50.2005
2	31.302	MF	1.2420	3.66080e4	491.23166	49.7995

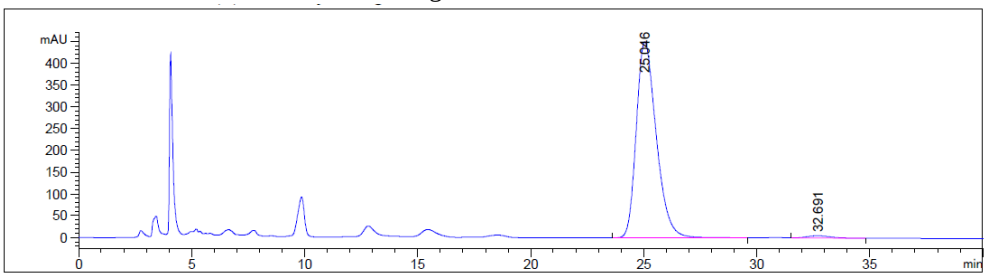
HPLC chromatogram of racemic **3aa**



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.958	MF	1.0007	1.84437e4	307.19296	97.7952
2	32.411	BB	0.9151	415.82068	5.37157	2.2048

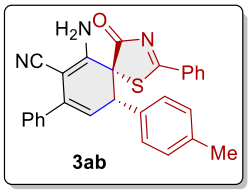
HPLC chromatogram of enantioenriched **3aa**

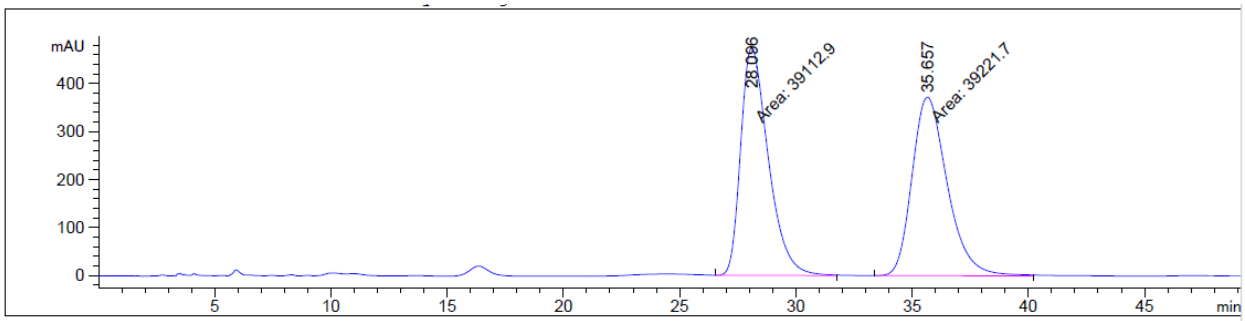


Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.046	BB	0.9419	2.75970e4	449.71899	98.5956
2	32.691	BB	0.8866	393.10608	5.24392	1.4044

HPLC chromatogram of enantioenriched **3aa (scale-up)**

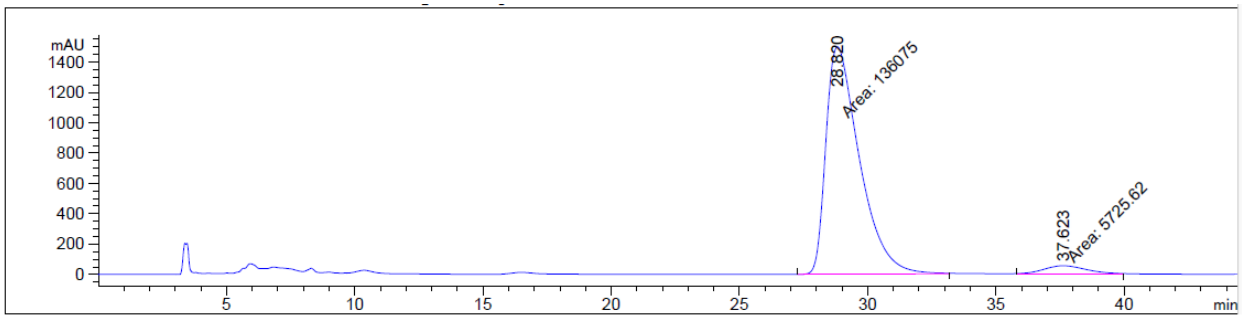




Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.096	MF	1.3774	3.91129e4	473.26801	49.9306
2	35.657	MF	1.7596	3.92217e4	371.49149	50.0694

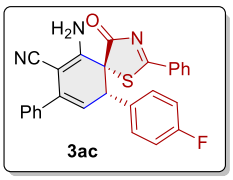
HPLC chromatogram of racemic **3ab**

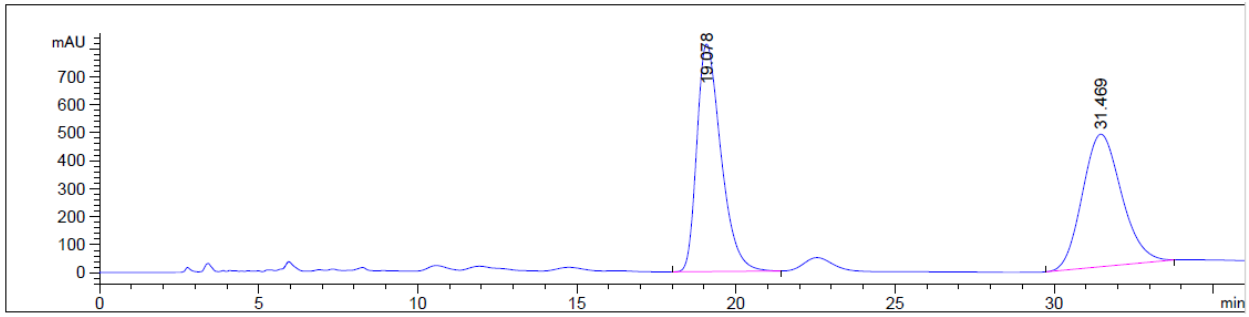


Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.820	MF	1.5144	1.36075e5	1497.51648	95.9622
2	37.623	MM	1.8464	5725.62402	51.68310	4.0378

HPLC chromatogram of enantioenriched **3ab**

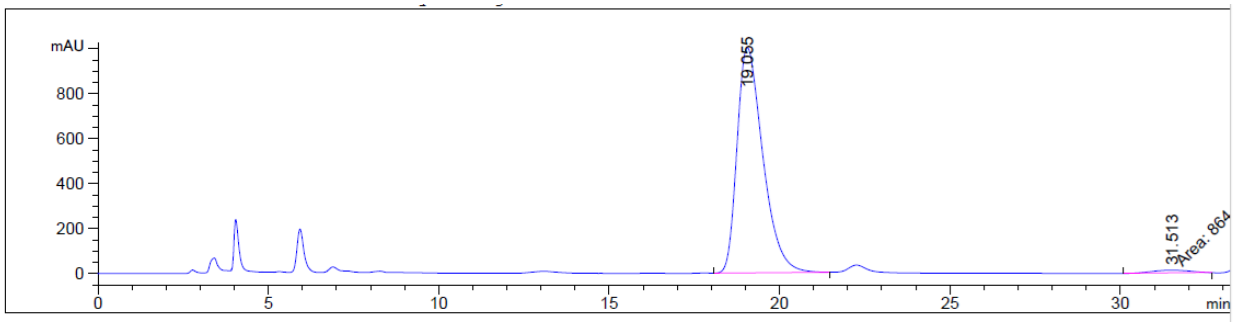




Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.078	BB	0.8083	4.28006e4	812.86743	51.4282
2	31.469	BB	1.3195	4.04233e4	473.74359	48.5718

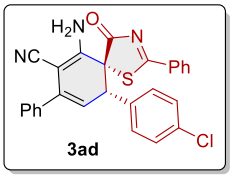
HPLC chromatogram of racemic **3ac**

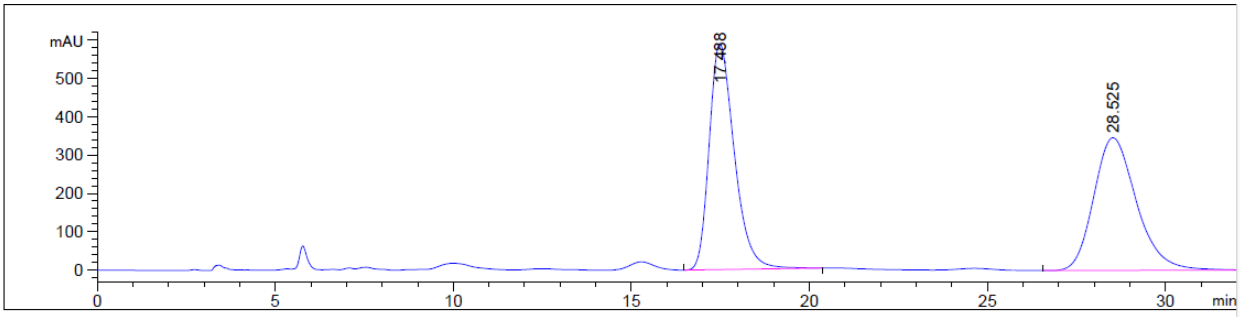


Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.055	BB	0.8083	5.27711e4	1002.16754	98.3883
2	31.513	MM	0.8865	864.41809	12.05620	1.6117

HPLC chromatogram of enantioenriched **3ac**

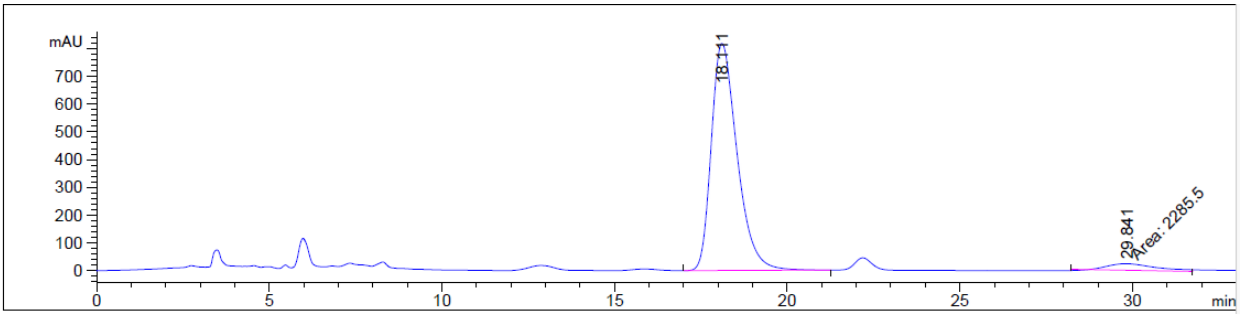




Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.488	BB	0.7526	2.89654e4	590.15472	50.0213
2	28.525	BB	1.2742	2.89407e4	346.58884	49.9787

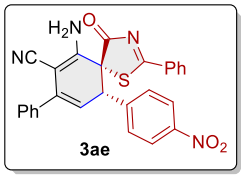
HPLC chromatogram of racemic **3ad**

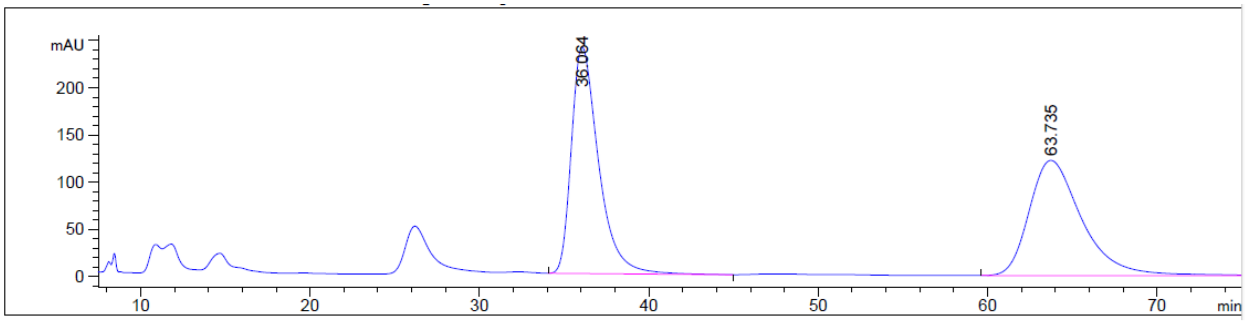


Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.111	BB	0.7976	4.24027e4	816.84729	94.8857
2	29.841	MM	1.6268	2285.49585	23.41451	5.1143

HPLC chromatogram of enantioenriched **3ad**

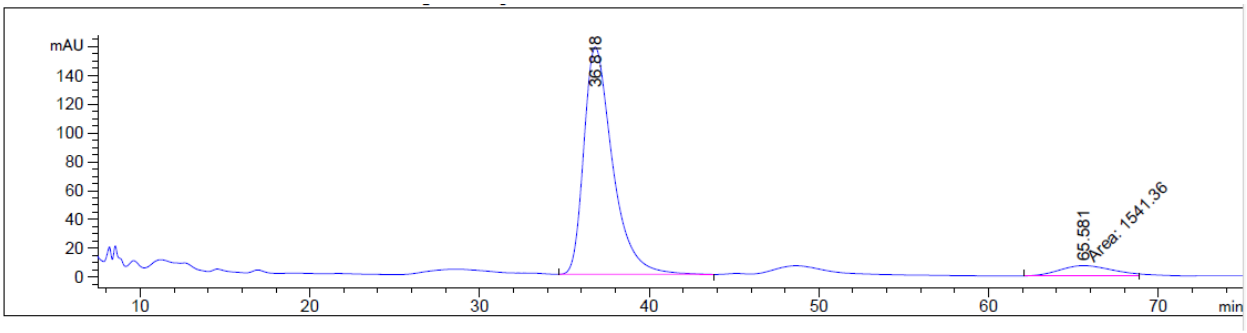




Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	36.064	BB	1.6623	2.68470e4	240.13925	50.2283
2	63.735	BB	2.5565	2.66029e4	122.07000	49.7717

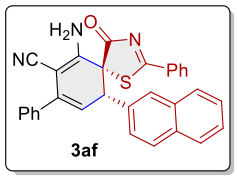
HPLC chromatogram of racemic **3ae**

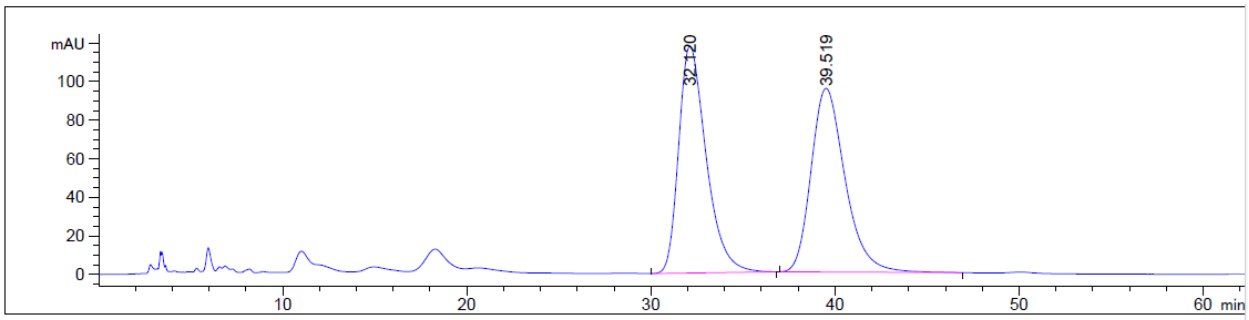


Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	36.818	BB	1.7353	1.85507e4	157.82019	92.3285
2	65.581	MF	3.5953	1541.36450	7.14529	7.6715

HPLC chromatogram of enantioenriched **3ae**

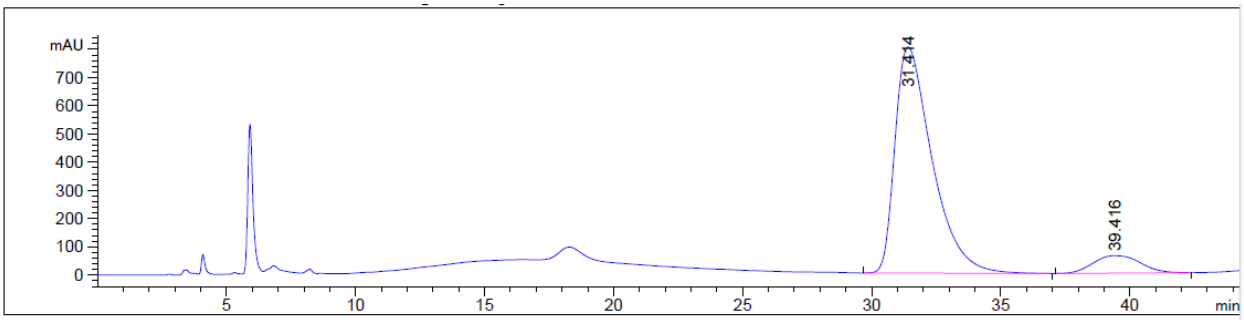




Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	32.120	BB	1.5401	1.22461e4	117.87425	50.0047
2	39.519	BB	1.8307	1.22438e4	95.31220	49.9953

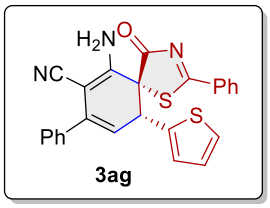
HPLC chromatogram of racemic **3af**

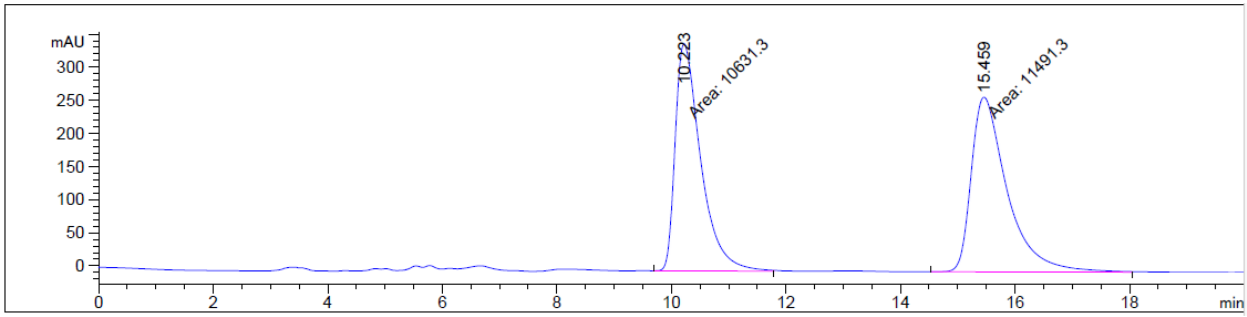


Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	31.414	BB	1.5081	7.99681e4	801.47815	91.0520
2	39.416	BB	1.7067	7858.72266	62.00407	8.9480

HPLC chromatogram of enantioenriched **3af**

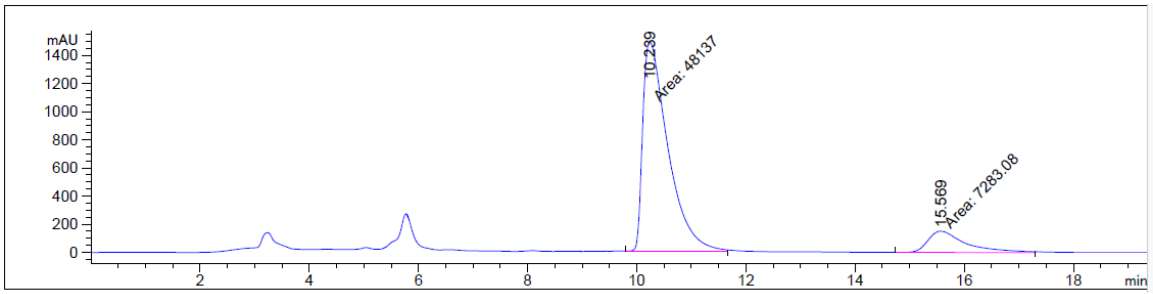




Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.223	MF	0.5165	1.06313e4	343.05524	48.0564
2	15.459	MF	0.7258	1.14913e4	263.86594	51.9436

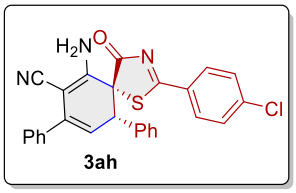
HPLC chromatogram of racemic **3ag**

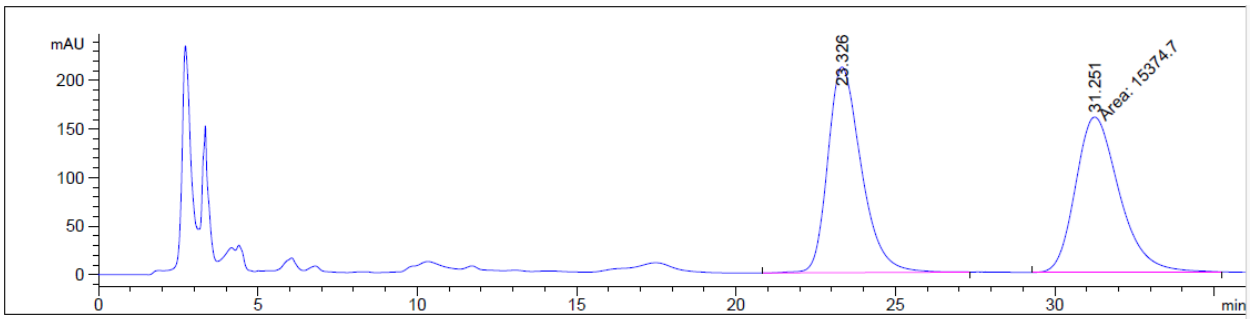


Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.239	MF	0.5372	4.81370e4	1493.48926	86.8584
2	15.569	MF	0.8037	7283.07568	151.03822	13.1416

HPLC chromatogram of enantioenriched **3ag**

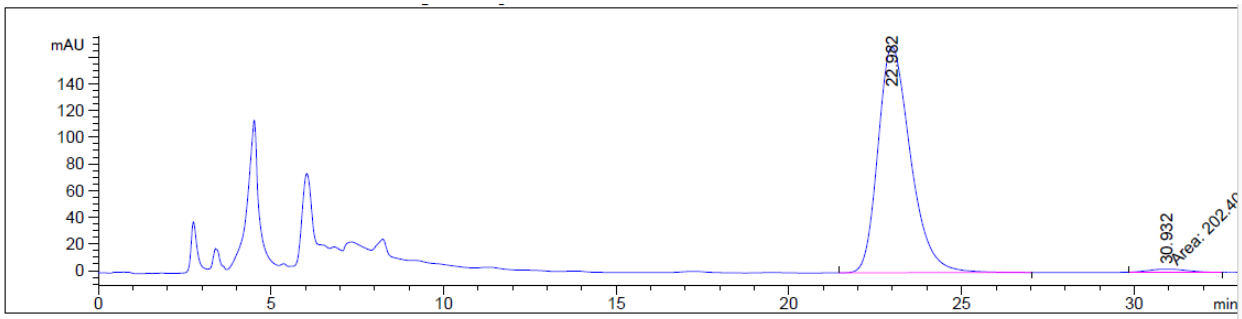




Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.326	BB	1.1181	1.54737e4	211.85439	50.1605
2	31.251	MF	1.6006	1.53747e4	160.09740	49.8395

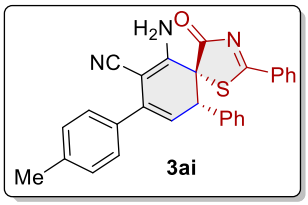
HPLC chromatogram of racemic **3ah**

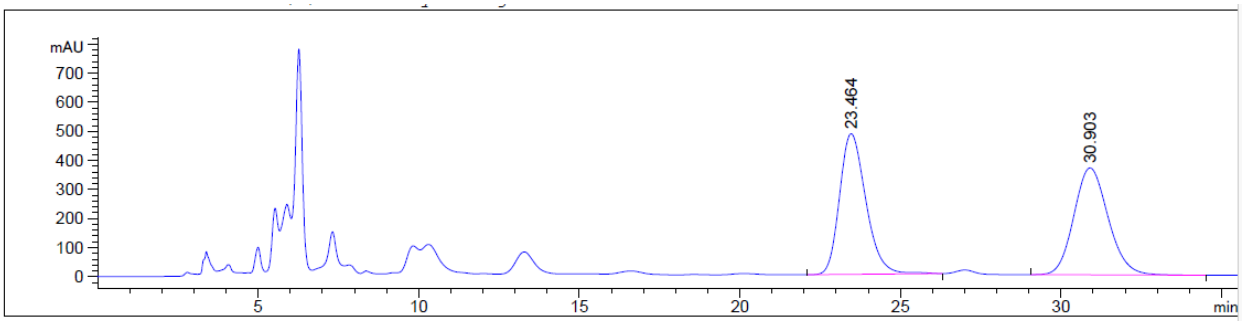


Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.982	BB	0.9943	1.10906e4	169.30002	98.2077
2	30.932	MM	1.3216	202.40193	2.55253	1.7923

HPLC chromatogram of enantioenriched **3ah**

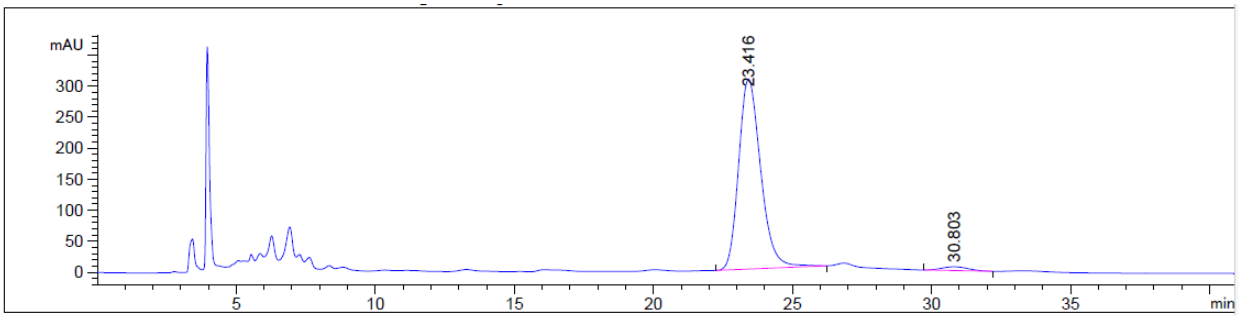




Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.464	BB	0.8787	2.75781e4	484.02240	50.2476
2	30.903	BB	1.1442	2.73062e4	367.78412	49.7524

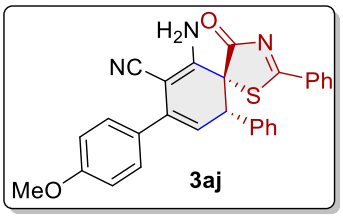
HPLC chromatogram of racemic **3ai**

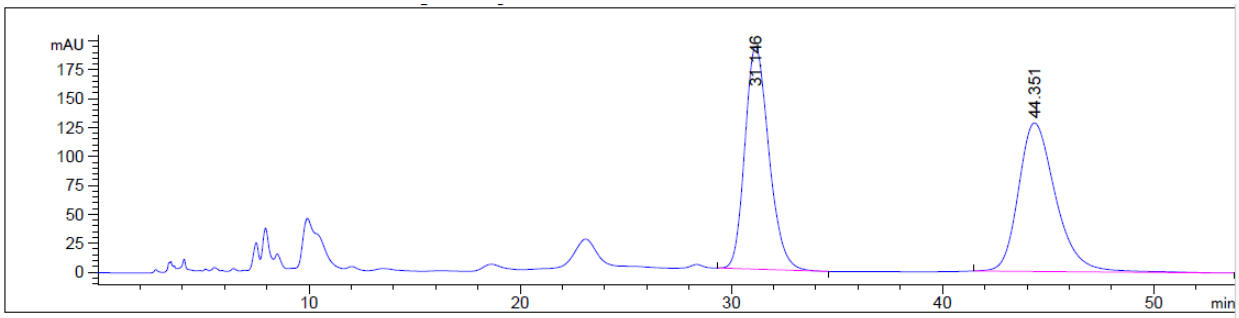


Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.416	BB	0.8460	1.68705e4	306.55765	97.7075
2	30.803	BB	0.7783	395.83395	6.07392	2.2925

HPLC chromatogram of enantioenriched **3ai**

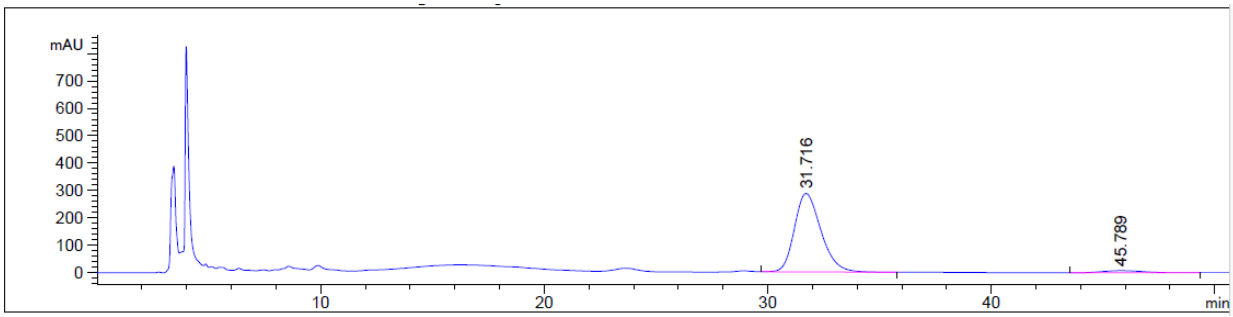




Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	31.146	BB	1.2055	1.51911e4	192.31912	49.1216
2	44.351	BBA	1.7238	1.57344e4	128.39061	50.8784

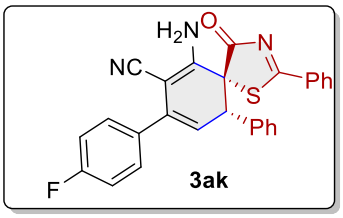
HPLC chromatogram of racemic **3aj**

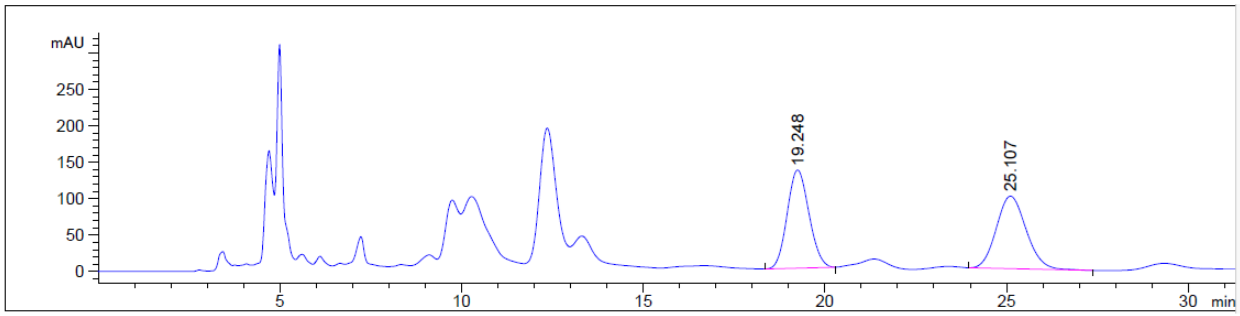


Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	31.716	BB	1.2552	2.35700e4	286.09360	95.9107
2	45.789	BB	1.5024	1004.93823	7.89837	4.0893

HPLC chromatogram of enantioenriched **3aj**

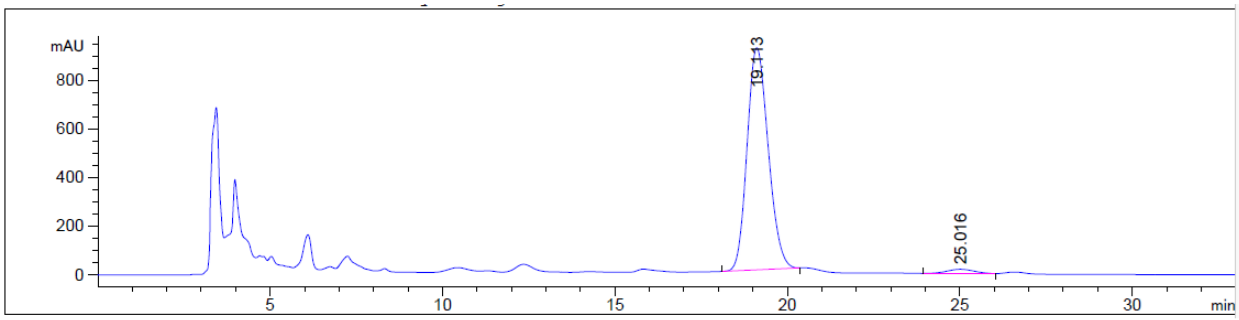




Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.248	BB	0.6482	5621.19385	134.88457	49.6854
2	25.107	BB	0.8781	5692.38477	99.70365	50.3146

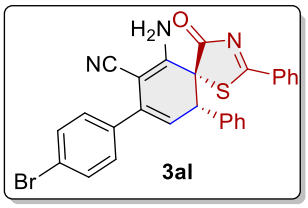
HPLC chromatogram of racemic **3ak**

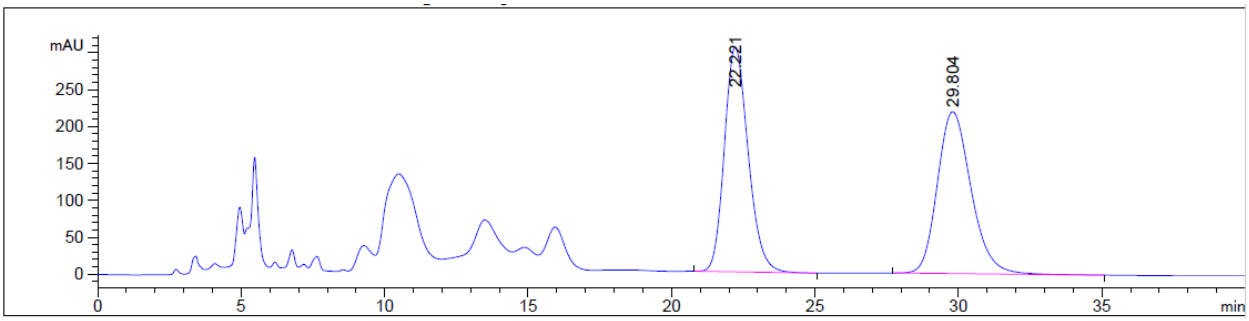


Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.113	BB	0.6607	3.89066e4	913.78870	97.7032
2	25.016	BB	0.7598	914.61896	17.10519	2.2968

HPLC chromatogram of enantioenriched **3ak**

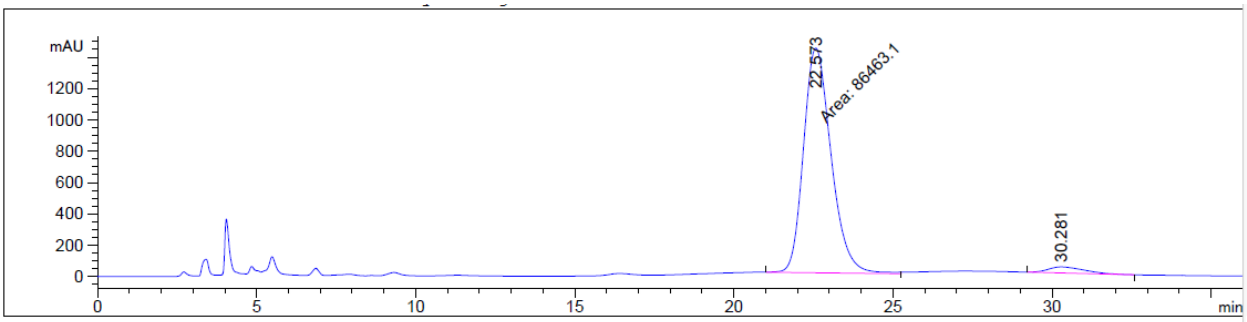




Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.221	BB	0.8936	1.75743e4	304.36880	49.5315
2	29.804	BB	1.2525	1.79067e4	219.31947	50.4685

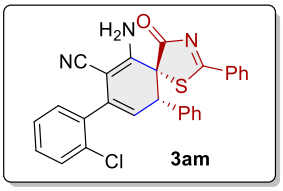
HPLC chromatogram of racemic **3al**

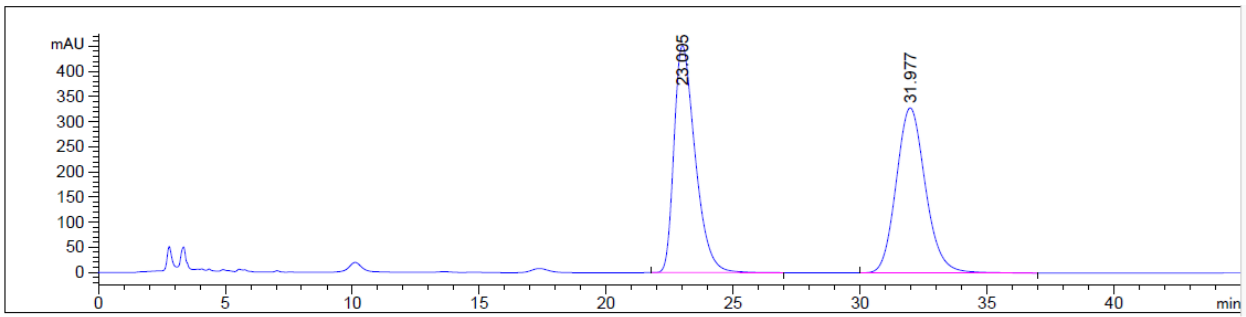


Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.573	MM	1.0051	8.64631e4	1433.78857	96.6743
2	30.281	BBA	1.0733	2974.42920	38.16445	3.3257

HPLC chromatogram of enantioenriched **3al**

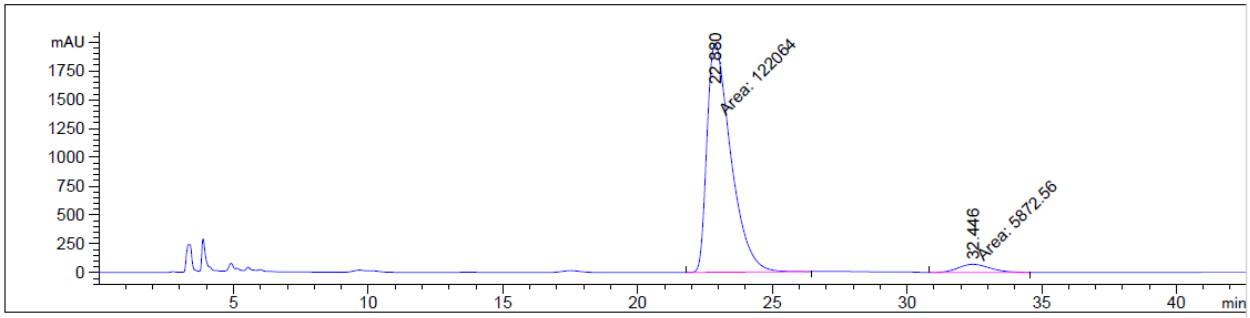




Signal 1: DAD1 A, Sig=250,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.005	BB	0.8846	2.62190e4	452.11755	49.9730
2	31.977	BB	1.2281	2.62474e4	328.52502	50.0270

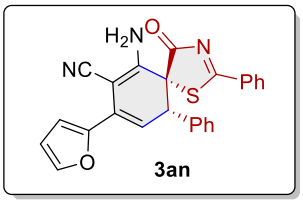
HPLC chromatogram of racemic **3am**

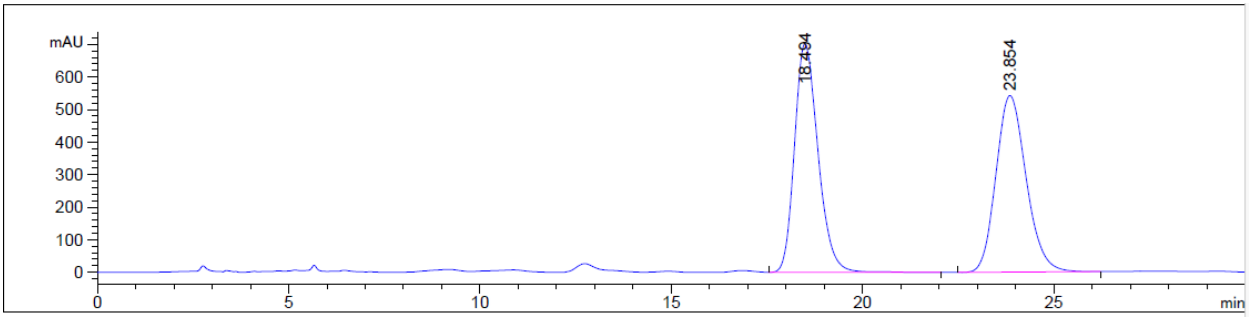


Signal 1: DAD1 A, Sig=250,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.880	MM	1.0256	1.22064e5	1983.56873	95.4098
2	32.446	MF	1.3811	5872.56201	70.86717	4.5902

HPLC chromatogram of enantioenriched **3am**

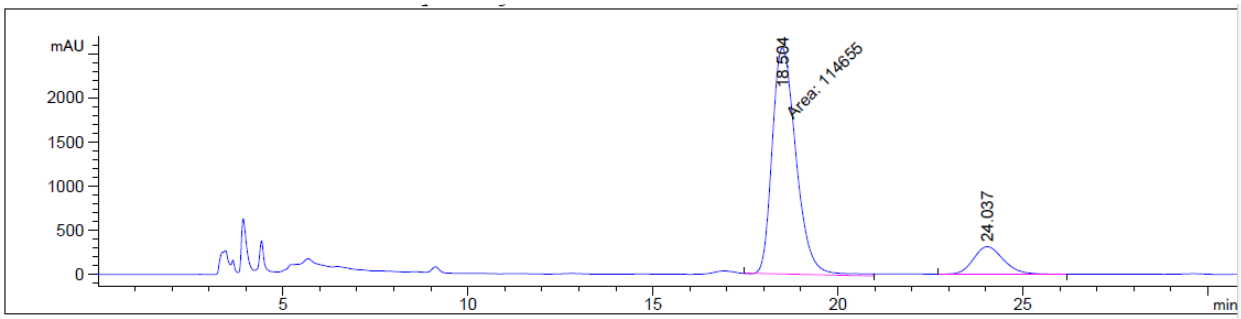




Signal 1: DAD1 A, Sig=250,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.494	BB	0.6592	3.00459e4	702.24933	50.2101
2	23.854	BB	0.8484	2.97945e4	542.82422	49.7899

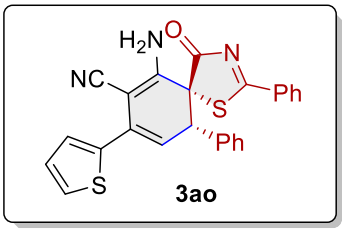
HPLC chromatogram of racemic **3an**

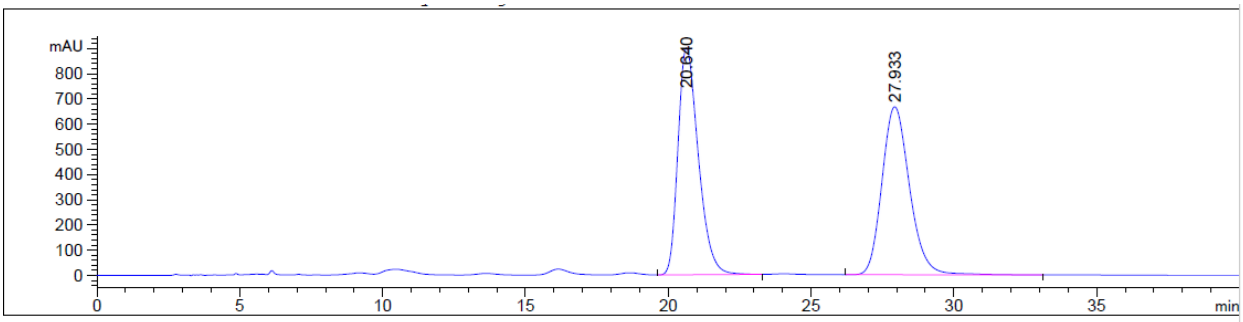


Signal 1: DAD1 A, Sig=250,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.504	MM	0.7470	1.14655e5	2558.20605	86.8188
2	24.037	BB	0.8654	1.74075e4	310.80289	13.1812

HPLC chromatogram of enantioenriched **3an**

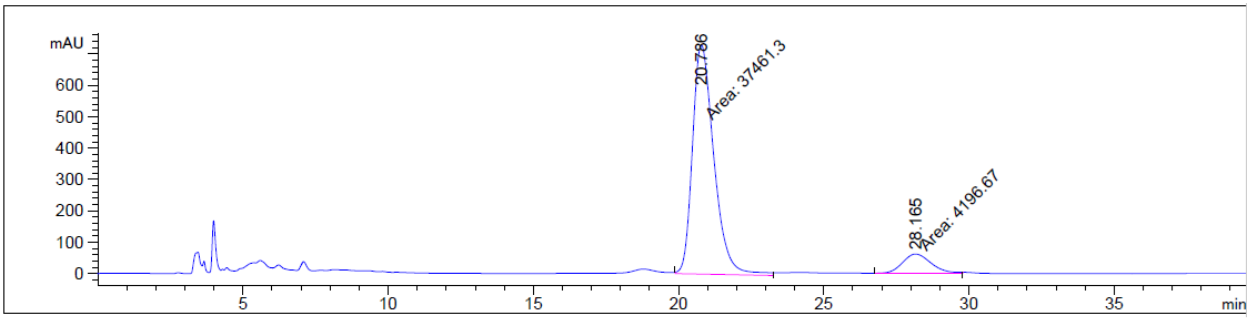




Signal 1: DAD1 A, Sig=250,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.640	BB	0.7640	4.45914e4	900.01019	49.8957
2	27.933	BB	1.0379	4.47778e4	666.42883	50.1043

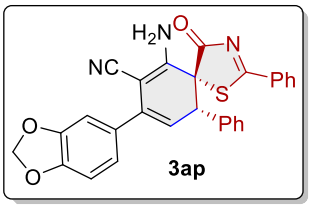
HPLC chromatogram of racemic **3ao**

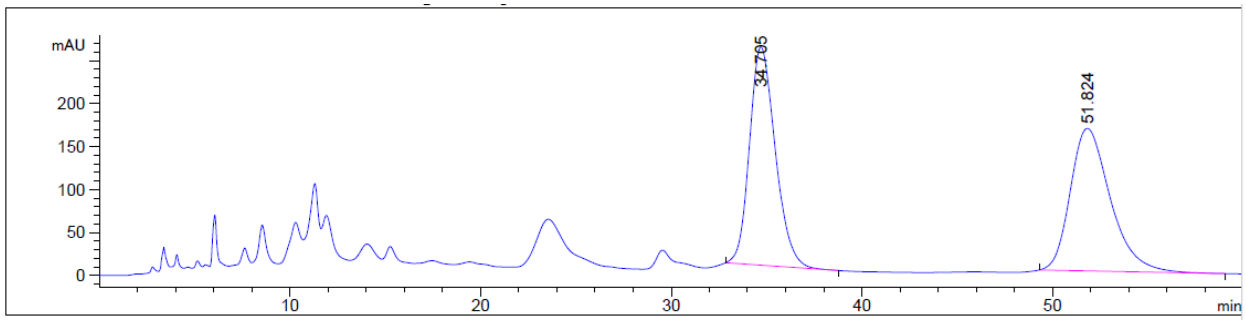


Signal 1: DAD1 A, Sig=250,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.786	MM	0.8551	3.74613e4	730.13049	89.9259
2	28.165	MF	1.1400	4196.66748	61.35361	10.0741

HPLC chromatogram of enantioenriched **3ao**

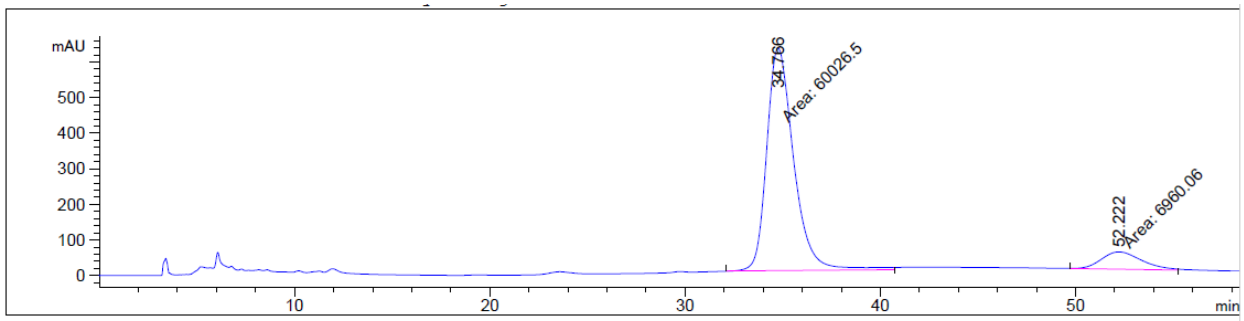




Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	34.705	BB	1.3646	2.38513e4	253.76091	49.6442
2	51.824	BB	2.0429	2.41932e4	165.74669	50.3558

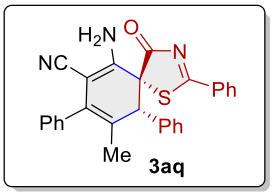
HPLC chromatogram of racemic **3ap**

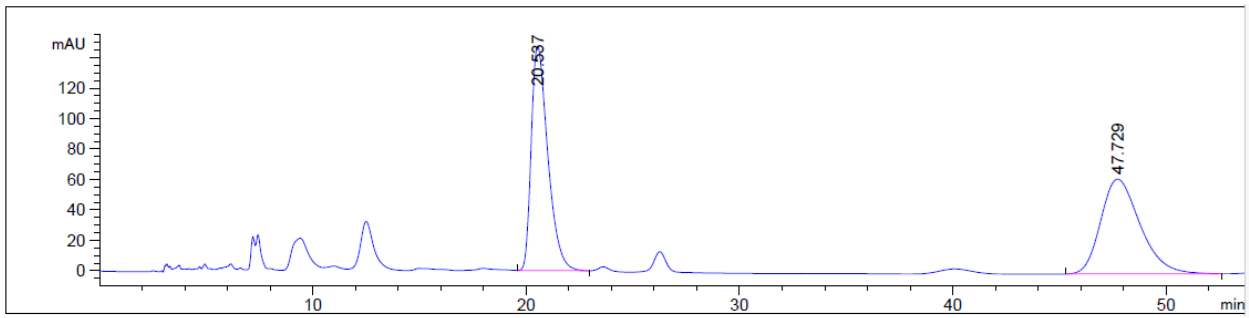


Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	34.766	MM	1.5994	6.00265e4	625.51733	89.6098
2	52.222	MF	2.3805	6960.05615	48.72953	10.3902

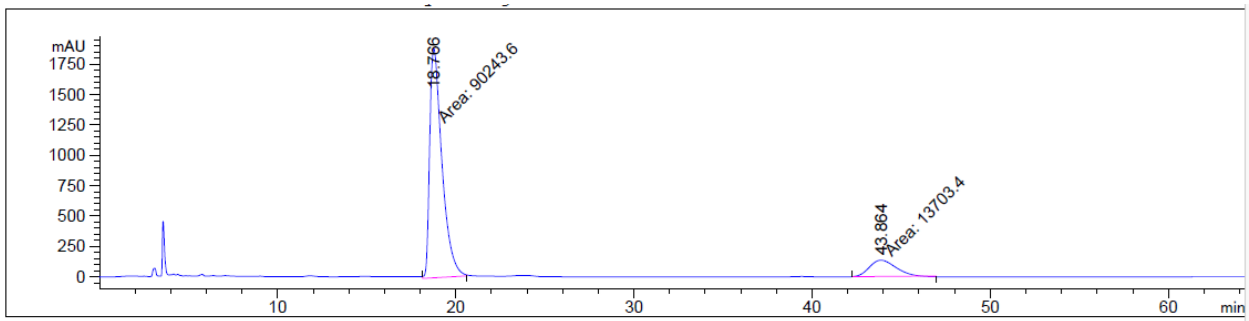
HPLC chromatogram of enantioenriched **3ap**





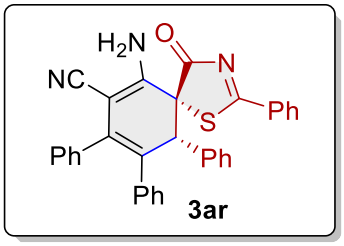
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.537	BB	0.8224	7971.19678	147.51506	49.9153
2	47.729	BB	1.5746	7998.26172	62.34973	50.0847

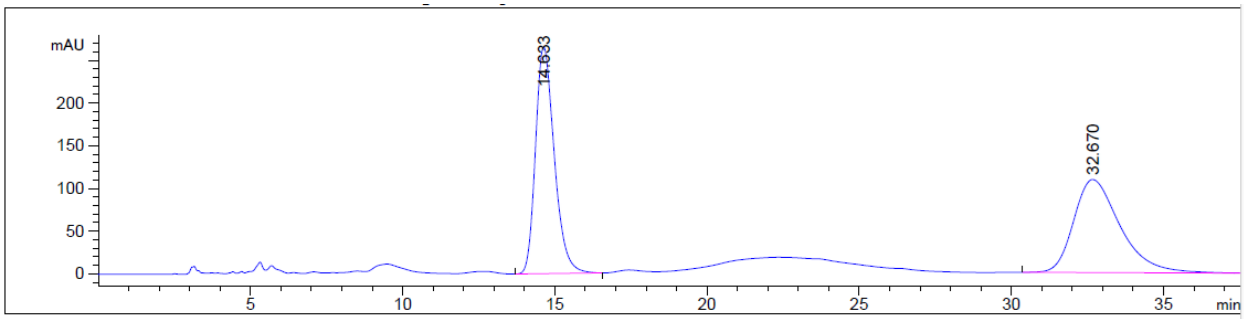
HPLC chromatogram of racemic **3aq**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.766	MM	0.7960	9.02436e4	1889.53442	86.8169
2	43.864	MM	1.7079	1.37034e4	133.72675	13.1831

HPLC chromatogram of enantioenriched **3aq**

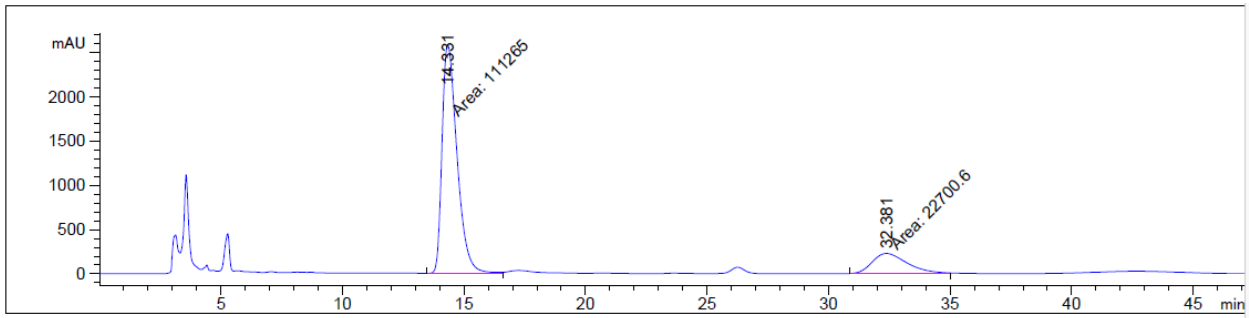




Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.633	BB	0.6628	1.14044e4	265.69263	49.7316
2	32.670	BBA	1.5524	1.15275e4	108.94885	50.2684

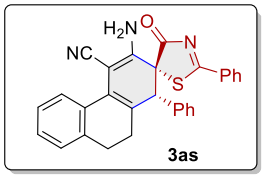
HPLC chromatogram of racemic **3ar**

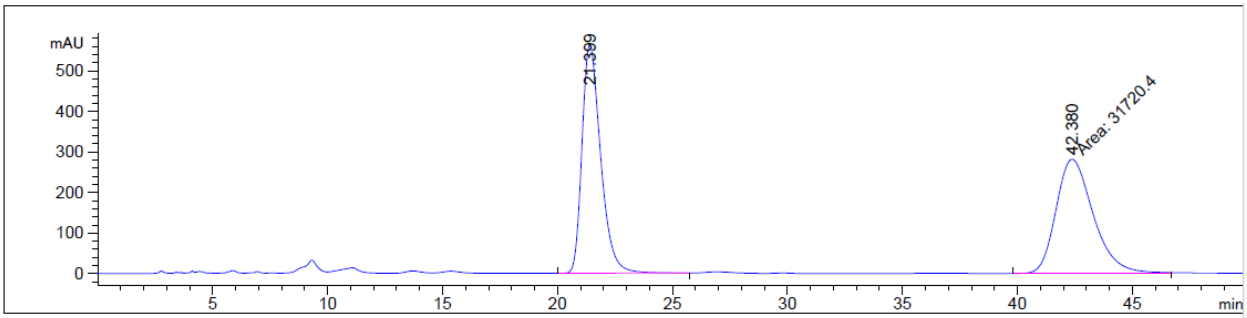


Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.331	MM	0.7175	1.11265e5	2584.59888	83.0549
2	32.381	MM	1.6699	2.27006e4	226.56496	16.9451

HPLC chromatogram of enantioenriched **3ar**

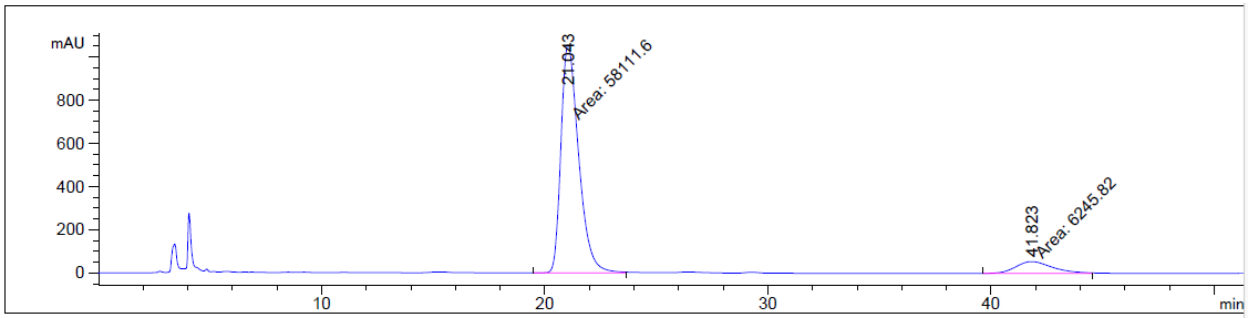




Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.399	BB	0.8599	3.17420e4	562.85950	50.0170
2	42.380	MF	1.8782	3.17204e4	281.48090	49.9830

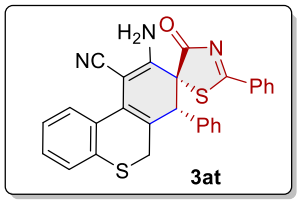
HPLC chromatogram of racemic **3as**

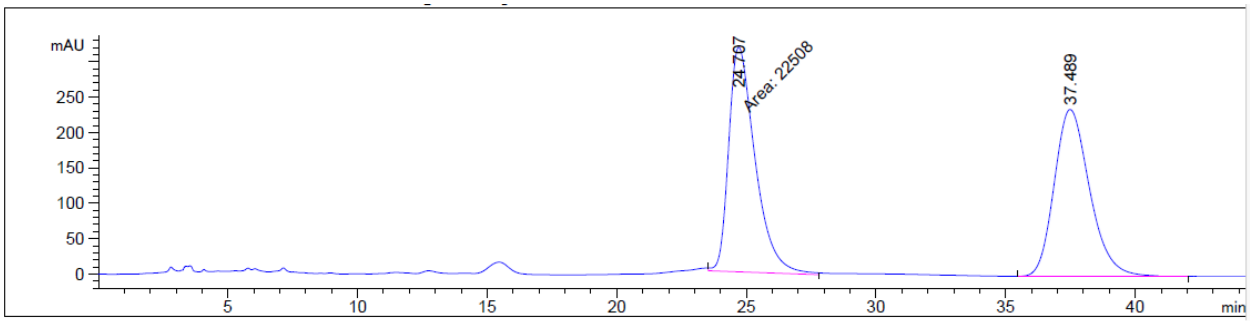


Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.043	MF	0.9174	5.81116e4	1055.75635	90.2951
2	41.823	MF	1.9124	6245.82031	54.43129	9.7049

HPLC chromatogram of enantioenriched **3as**

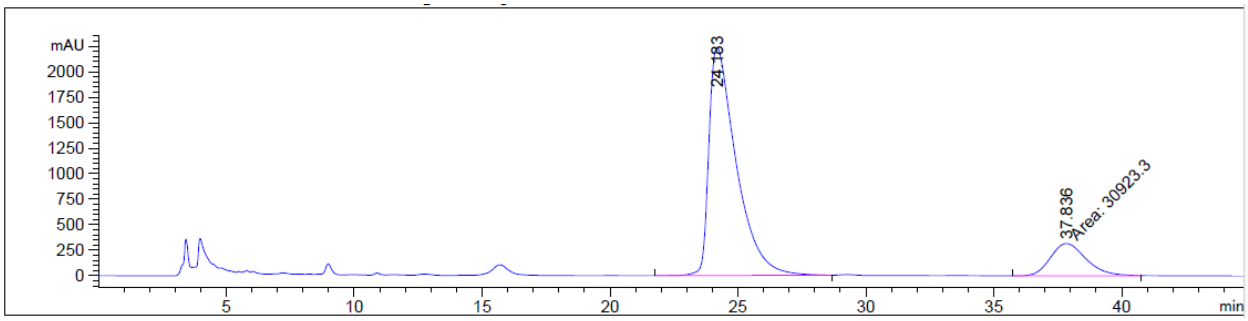




Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.707	MM	1.1821	2.25080e4	317.35568	50.1450
2	37.489	BB	1.3932	2.23779e4	235.79112	49.8550

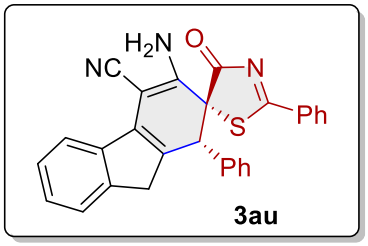
HPLC chromatogram of racemic **3at**

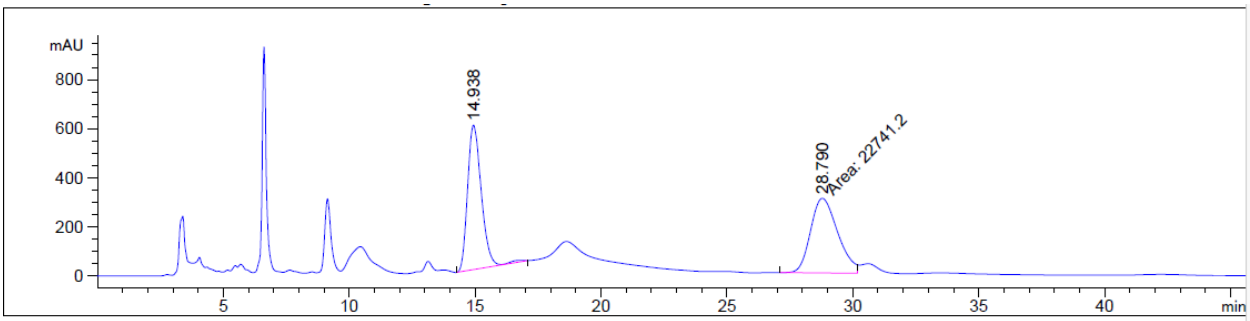


Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.183	BB	0.9727	1.65989e5	2239.65918	84.2959
2	37.836	MF	1.6242	3.09233e4	317.31750	15.7041

HPLC chromatogram of enantioenriched **3at**

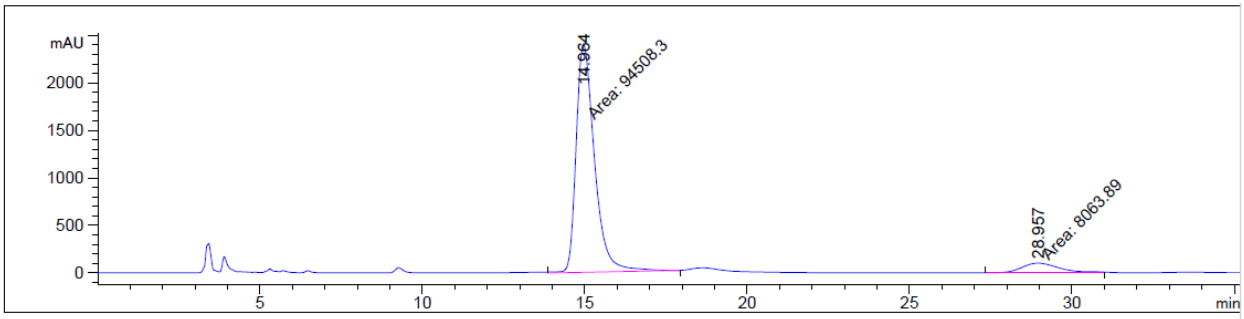




Signal 1: DAD1 A, Sig=250,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.938	BV R	0.5817	2.23486e4	588.72455	49.5647
2	28.790	MF	1.2461	2.27412e4	304.17151	50.4353

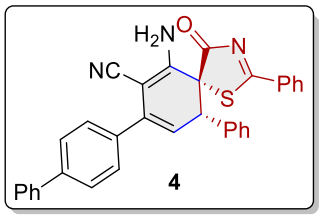
HPLC chromatogram of racemic **3au**

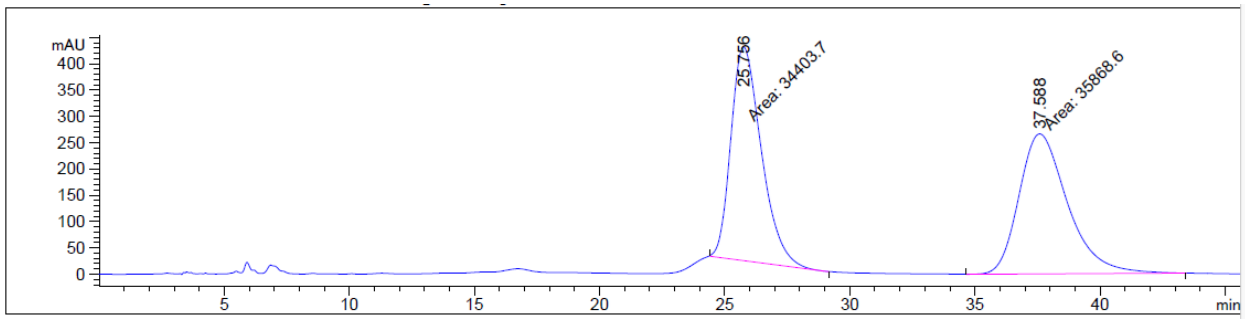


Signal 1: DAD1 A, Sig=250,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.964	MM	0.6575	9.45083e4	2395.60498	92.1383
2	28.957	MF	1.3314	8063.89111	100.94608	7.8617

HPLC chromatogram of enantioenriched **3au**

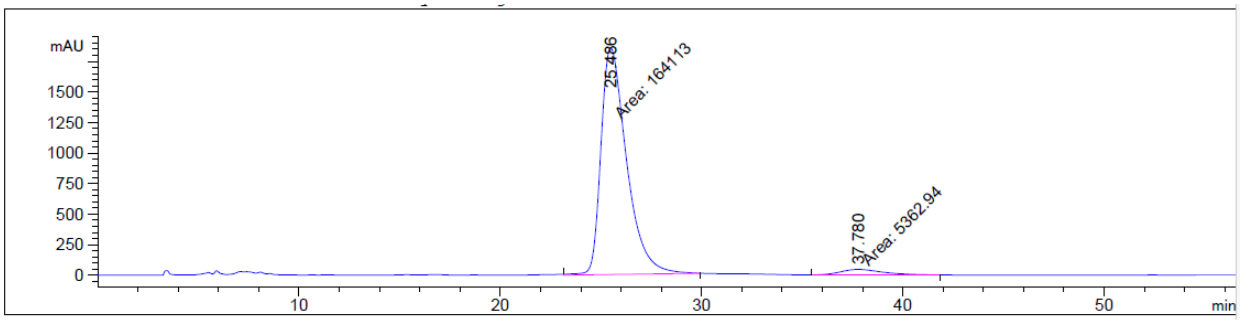




Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.756	MM	1.4109	3.44037e4	406.39673	48.9576
2	37.588	MM	2.2467	3.58686e4	266.08871	51.0424

HPLC chromatogram of racemic **4**



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.486	MM	1.4749	1.64113e5	1854.45703	96.8356
2	37.780	MM	2.1624	5362.93555	41.33546	3.1644

HPLC chromatogram of enantioenriched **4**